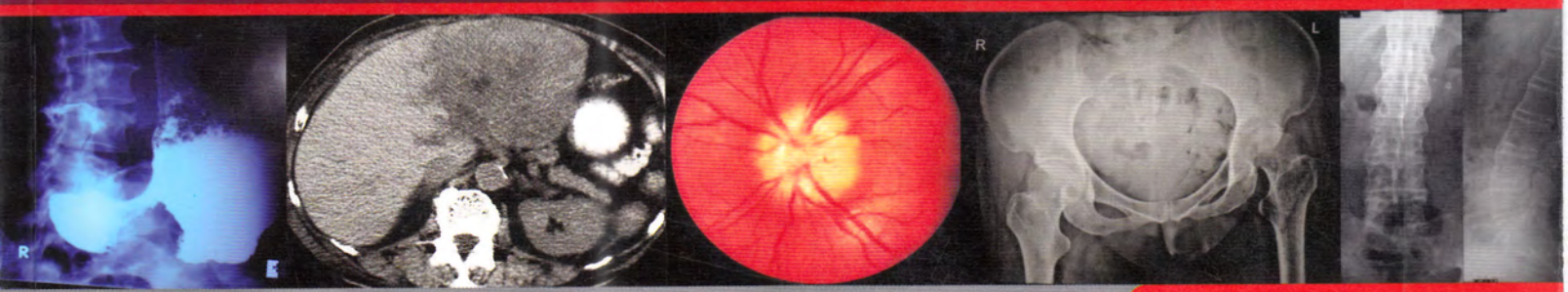
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Short Cases in CLINICAL MEDICINE



FIFTH EDITION

ABM Abdullah

Foreword by
Prof. Ramesh C. Deka

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Short Cases in Clinical Medicine

Fifth Edition

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Section A

Short Cases

CHAPTER 1

General Examination

"Doctors must be good observants like detectives"

– Author's View

Introduction

During examination of short case, examiner usually asks to examine a particular part of the body, or sometimes the whole system or whole body. Candidates should prepare themselves to examine accordingly, but systematically. Common instructions by the examiner or short cases in any examinations are:

1. **General examination:** Perform the general examination of this patient.
2. **In cardiovascular system (CVS):**
 - Examine the precordium.
 - Palpate and auscultate the precordium.
 - Examine the pulse.
 - Examine the CVS.
3. **In respiratory system:**
 - Examine the chest (front or back or both).
 - Auscultate for respiratory system.
 - Percuss the back and auscultate.
4. **Abdomen:**
 - Examine the abdomen.
 - Palpate the abdomen and relevant.
 - Examine the gastrointestinal system.
5. **Neurology:**
 - Examine the lower limb or upper limb.
 - Examine the cranial nerves, or a particular cranial nerve (e.g. facial nerve).
 - Show me the cerebellar signs.
 - Look at the gait of the patient.
6. **Endocrinology:**
 - Examine the neck (mostly thyroid).
 - Examine the thyroid gland and relevant (thyroid disorder and features of hyper- or hypothyroidism).
 - Look at the face (thyrotoxic, myxoedematous or Cushingoid).
 - Perform the general examination (obesity, features of myxoedema, pigmentation in Addison disease).
7. **Rheumatology:**
 - Examine the hands (mostly rheumatoid hand, systemic sclerosis).
 - Examine the knee joints (or any particular joint—monoarthritis, or polyarthritis, effusion in knee joints).
 - Examine the face and relevant [features of systemic sclerosis, systemic lupus erythematosus (SLE), dermatomyositis].
 - Look at the skin (dermatomyositis).
8. **Dermatology:**
 - Perform the general examination (psoriasis, exfoliative dermatitis).
 - Look at the skin of this part. What are the possibilities (skin rash, erythema multiforme, purpura, Stevens–Johnson syndrome, blisters)?
9. **Eyes:**
 - Examine the eyes [ptosis, squint, pigmentation of sclera, **Kayser–Fleischer** (KF) ring, corneal arcus, subconjunctival haemorrhage, exophthalmos].
 - Perform fundoscopy (optic atrophy, retinopathy).
10. **Miscellaneous:**
 - Depends on particular type of case, e.g. Turner syndrome, Down syndrome, xanthelasma, etc.

- Look at the tongue. What is the diagnosis? What are the diseases that can be diagnosed by looking at the tongue?
- Look at the face. Name some diseases that can be diagnosed by looking at the face.
- Examine the hands. What are the diseases that can be diagnosed by examining the hands?
- What diseases are diagnosed by looking at the nail?

General Examination

Be sure that you are on the right side of the patient. Introduce yourself, ask for permission, and be gentle and polite. A friendly handshake may offer patient's reassurance and cooperation, also may help to get informations such as warm and sweaty hands (**thyrotoxicosis**), cold and sweaty hands (**anxiety**), dry and coarse hands (**hypothyroid**), doughy feeling (**acromegaly**) and slow relaxation of grip (**myotonia**).

Before starting the examination, take a few moments to look quickly from head to foot (by keeping open your **wide-angled lens**), which may give a clue regarding the diagnosis. Many cases can be diagnosed by just looking at a glance (such as emaciation or cachexia, obesity, acromegaly, myxoedema and Cushing syndrome).

Facial expression will give a good clue for the diagnosis (see page 502), for example:

- Poverty in expression or mask-like face (in Parkinsonism).
- Agitated or terror face (in thyrotoxicosis).
- Exophthalmos (in Graves disease).
- Puffy face (in myxoedema or nephrotic syndrome).
- Apathy (in depression).

Look at the **height**:

- Tall stature (gigantism, Marfan syndrome, Klinefelter syndrome).
- Short stature (constitutional, genetic or familial, achondroplasia, cretinism or juvenile hypothyroidism, hypopituitarism).

Besides routine general examination, some extra findings in individual cases should be seen. For example:

- In **Cushing syndrome**, some extra findings are very essential, e.g. **striae, moon face and buffalo hump**.
- If **butterfly rash** is seen on the face, check for rash in other parts of the body. Also, **heliotrope rash** and **alopecia**.



Cachexia

Main Points in General Examination

- **Appearance** (ill-looking, depressed, anxious, Cushingoid or expressionless face).
- **Built** (obese, emaciated or cachexic, tall, short or normal).
- **Nutrition** (well nourished, poor or normal).
- **Decubitus** (on choice, propped up or Mohammedan prayer position).
- **Anaemia** (palpebral part of conjunctiva, tongue, palm, nails and whole body).
- **Jaundice** (sclera, undersurface of tongue, palm or whole body).
- **Cyanosis** (tip of nose, lips, ear lobule, tongue, tip of fingers and toes).



Tall stature (Marfan syndrome)



Nail (leuconychia)



Jaundice

- **Clubbing** (see fluctuation of nail base, angle between the nail and its base, curvature of nails, look for hypertrophic osteoarthropathy by pressing the lower end of tibia–fibula or radius–ulna. Be aware of differential clubbing—it means clubbing in toes but not in fingers).
- **Koilonychia** (dryness, brittleness, flattening, thinning and spooning of nails).
- **Leuconychia** (white spots or white nail).
- **Oedema** (in leg above medial malleolus, sacrum if the patient is recumbent).
- **Dehydration** (skin turgor or dry tongue).
- **Pigmentation** (exposed parts, face, neck, palmar creases, knuckles, inner side of mouth or recent scar).
- **Lymph nodes** (examine systematically in different areas).
- **Thyroid gland** (if enlarged, examine in detail and see the features of toxicosis or hypothyroidism).
- **Breasts.**
- **Body hair distribution** (including head to see alopecia).
- **Pulse.**
- **Blood pressure (BP).**
- **Temperature.**
- **Respiratory rate.**

Relevant findings should be examined according to individual cases, for example:

1. **In the face:** If xanthelasma is present, see corneal arcus, xanthomatous nodules in others parts (elbow, knees, extensor surfaces, Achilles tendon and palmar creases).
2. **In the hands:**
 - Dupuytren contracture.
 - Palmar erythema.
 - Osler node and splinter haemorrhage [in subacute bacterial endocarditis (SBE)].
 - Heberden node.
 - Bouchard node.
 - Gangrene or nail fold infarct or nail fold telangiectasia.
 - Ulceration.
 - Wasting.
 - Skin rash or Gottron patch (dermatomyositis).
3. **Other findings:**
 - Spider angioma.
 - Parotid gland enlargement (unilateral or bilateral).
 - Skin rash.
 - Striae.
 - Campbell de Morgan spots.
 - Purpura.
 - Vitiligo.
 - Deformity (kyphosis, scoliosis and lordosis).

If these findings are present, you must mention them.

N.B. Mention, if the patient has any cannula, catheter, nasogastric (NG) tube, central venous (CV) line, arteriovenous (AV) fistula, etc.

Never forget to examine the lower limbs (there may be unilateral leg swelling, deep vein thrombosis [DVT], differential cyanosis, differential clubbing, trophic ulcer, gangrene or infarction at the tip of toe).

Finally, present the case systematically. Remember, you must follow the examiner's instructions, For example, examiner may ask:

- What are your findings? (You should mention the positive and important negative findings.)
- Have you finished your examination? Now tell about your findings. (You should tell systematically the positive and important negative findings.)

Examples of Presentation of a Case

Case No. 1

- The patient is ill-looking, emaciated or cachexic with poor nutrition.
- Mildly anaemic, nonicteric and noncyanosed.
- There is clubbing involving all the fingers and toes, no leuconychia and no oedema.
- Thyroid gland is normally palpable and there is no lymphadenopathy.
- He is normally pigmented.
- Pulse: 80/min, BP: 120/8 mmHg, respiration: 18/min and temperature: normal.

Examiner may ask:

Q: What are the **causes of cachexia** in this elderly patient?
A: Tuberculosis, diabetes mellitus, thyrotox-icosis, malignancy, malnutrition or malabsorption.

Q: What are the **causes of cachexia** in this young lady?
A: Tuberculosis (TB), diabetes mellitus (DM), thyrotoxicosis, malnutrition or malabsorption, anorexia nervosa, Addison disease.

Q: What are the **causes of clubbing** in this case?
A: See later in the topic 'clubbing'.

Case No. 2

- This patient is obese, mildly anaemic, nonicteric, noncyanosed.
- No clubbing, koilonychia or leuconychia.

Examiner may ask:

Q: What do you think are the **causes of obesity?** What **else** do you like to see in obesity?
A: I want to look for striae, central obesity, moon face and buffalo hump (in Cushing syndrome). For details, see in the topic 'obesity'.

Case No. 3

- The patient has generalised lymphadenopathy (tell the site and size that are firm, discrete, nontender, not fixed with overlying skin or underlying structure).

Q: What are the **causes of generalised lymphadenopathy?**
A: See later in lymphadenopathy.

Case No. 4

The patient is tall, lean and thin.

Examiner may ask:

Q: Look at the patient. What are your findings?
A: The patient is tall, lean and thin; extremities are long, face is narrow and elongated; arachnodactyly (long, elongated fingers)—likely to be a case of **Marfan syndrome**.

Q: What **else** do you like to examine?
A: I want to examine the eyes (dislocated lens), heart (aortic regurgitation), high-arched palate, arm span and height.

Case No. 5

The patient is tall and obese.

Examiner may ask:

Q: Look at this patient. What **else** do you want to see?
A: I want to see gynaecomastia, testis (atrophy), secondary sex characters and voice. This may be a case of **Klinefelter syndrome**.

Case No. 6

Young patient appearing pigmented.

Q: What **else** do you want to see?
A: Blood pressure (low in Addison disease. I want to see BP at both standing and lying position to see postural hypotension) and also I want to see pigmentation in other parts of the body (such as inner side of mouth, palmar crease, recent scar).

Case No. 7

The patient has generalized oedema.

Q: What are the possibilities? What else do you want to examine?
A: Generalized oedema may be due to nephrotic syndrome, hypoproteinaemia, cirrhosis of the liver, etc. (For details, see the relevant topics later in the respective chapters.)

Some Important Topics in General Examination

Causes of Pallor (Face or Whole Body)

- Anaemia (the commonest cause).
- Hypopituitarism (or hypogonadism).
- Others:
 - Shock.
 - Syncope.
 - Left ventricular failure (LVF).

Causes of Yellow Body

- Jaundice (the commonest cause).
- Carotenaemia.

Causes of Carotenaemia

- Excess intake of carotene-containing food (carrot, mango and tomato).
- Hypothyroidism (due to impaired metabolism of carotene by liver).

Q: How to **differentiate** between jaundice and carotenaemia?

A: In jaundice, sclera is involved. In carotenaemia, sclera is not involved.

Cyanosis

It is the bluish discolouration of skin and mucous membrane due to increased amount of deoxygenated haemoglobin in the blood. Cyanosis is not seen until the **amount** of deoxygenated haemoglobin (Hb) is >5 gm%.



Cyanosis at fingers



Cyanosis at tip of nose and lip

Two types of cyanosis:

- **Peripheral:** Due to localised reduction of blood flow on exposure to cold causing capillary vasoconstriction (lip is blue in cold weather). Also, occurs in reduced cardiac output (heart failure or shock). Tongue is spared in peripheral cyanosis.

 Causes:
 - Exposure to cold.
 - Raynaud phenomenon.
 - Heart failure.

- **Central:** Either due to imperfect oxygenation of blood in lung or admixture of venous and arterial blood. It is evident when O_2 saturation falls below 80–85%. Best site to see is tongue.

 Causes:
 - Respiratory: There is defect in oxygenation of blood in the lungs:
 - Chronic obstructive pulmonary disease (COPD).
 - Severe pneumonia.
 - Acute severe bronchial asthma.
 - Massive pulmonary embolism.
 - Pulmonary infarction.
 - Diffuse parenchymal lung disease (DPLD).
 - **Cardiac:**
 - Cyanotic congenital heart disease: Fallot tetralogy, transposition of great vessels.
 - Shunt anomaly (right-to-left shunt called Eisenmenger syndrome): Atrial septal defect (ASD), ventricular septal defect (VSD), patent ductus arteriosus (PDA).
 - Heart failure.
 - Cardiogenic shock.
 - **Others**
 - High altitude (physiological).
 - Polycythaemia.

Q: What are the **differences** between central and peripheral cyanosis?

A: The differences between central and peripheral cyanosis are as follows:

Points	Central	Peripheral
Mechanism	Imperfect oxygenation of blood in lung or admixture of venous and arterial blood in heart disease.	Local vasoconstriction or reduction of arterial flow.
Cyanosis	Generalised	Localised
Affected part	Warm	Cold
Application of warm	Does not disappear	Disappears
Oxygen	Cyanosis may disappear in pulmonary case (except in right-to-left shunt)	Disappears
Tongue	Always involved	Never involved

Q: Why **tongue** is not involved in peripheral cyanosis?

A: Because tongue is always warm, and circulation is good in tongue.

Q: Why there is **no cyanosis** in severe anaemia?

A: Because in severe anaemia, Hb is low and fully saturated, no excess deoxygenated Hb (in polycythaemia, cyanosis may occur even in mild hypoxia).

Q: What is **enterogenous** cyanosis? How to **diagnose**?

A: Discolouration of skin due to the presence of abnormal pigments in blood, as in sulphaemoglobinaemia or methaemoglobinaemia. History of intake of some drugs (sulphonamide, phenacetin and dapsone). No dyspnoea in enterogenous cyanosis or no other respiratory symptoms.



Oedema (non-pitting)



Oedema (pitting)

Clubbing

Proceed as follows:

- First look whether gross clubbing is present or not.
- If not, look carefully at the angle between nail bed and skin margin at the level of the observer's eye (normal angle is 150° between nail and cuticle).
- Next, see the fluctuation at the nail bed.
- Place the corresponding opposite nails of both hands (normally, small gap is present; if clubbing, there is reduction or absence of the gap called **window sign or Schamroth sign**).
- Feel the terminal parts of fingers (bulbousness due to increased thickening of nail bed); also look at the nails to see convexity from side-to-side.
- In advance stage, drumstick and later parrot-beak appearance.
- Always see hypertrophic osteoarthropathy; press the ends of long bones (radius and ulna, tibia and fibula). Look at the face (patient winces due to pain).

N.B. You must look at both the fingers and toes.



Clubbing of all fingers



Clubbing in toes

Presentation of a Case

- This patient has generalised clubbing involving all the fingers and toes with drumstick appearance (or parrot beak) and hypertrophic osteoarthropathy (mention, if any).

Q: What else do you want to examine?
A: I want to take the family history of clubbing and to examine the respiratory system, heart and abdomen to find out the causes.

Q: What is Schamroth sign?
A: When finger nails of the corresponding fingers of each hand are placed against each other, normally there is a diamond-shaped gap between them called Schamroth sign. It is lost in finger clubbing.

Q: What are the causes of clubbing?
A: Tell the causes according to the age.

If the patient is middle-aged or elderly, the causes are:

1. Respiratory
 - Bronchial carcinoma (squamous cell type, unusual in small cell type).
 - Suppurative lung disease (bronchiectasis, lung abscess and empyema thoracis).
 - Fibrosing alveolitis (or ILD).
 - Pulmonary TB (in advanced stage with fibrosis).
 - Pleural mesothelioma.
2. Cardiac (SBE).
3. Others: Cirrhosis of liver, inflammatory bowel disease, familial (rare) and idiopathic.

If the patient is young or of early age, the causes are:

1. Respiratory
 - Suppurative lung disease (bronchiectasis and lung abscess).
 - Cystic fibrosis.
 - Pulmonary TB (in advanced stage with fibrosis).
2. Cardiac
 - SBE.
 - Fallot tetralogy (clubbing with cyanosis).
3. Others: Chronic liver disease (CLD) (Wilson disease and alpha-1-antitrypsin deficiency).

N.B. The commonest cause in the elderly is bronchial carcinoma and in young is bronchiectasis.

Q: What is differential clubbing? What are the causes?
A: It means clubbing in the toes, but not in the fingers.

Causes of differential clubbing

- PDA with reverse shunt (also there is cyanosis in toes, not in finger called differential cyanosis).
- Infected abdominal aortic aneurysm.
- Coarctation of abdominal aorta.

Causes of unilateral clubbing

- Axillary artery aneurysm.
- Bronchial arteriovenous aneurysm.
- Others: Aneurysm of ascending aorta, subclavian or innominate artery.

Causes of clubbing in a single finger

- Trauma (the commonest cause).
- Chronic tophaceous gout.
- Sarcoidosis.

Causes of clubbing with cyanosis

- Fibrosing alveolitis.
- Cyanotic heart disease (Fallot tetralogy).
- Cystic fibrosis.
- Bilateral extensive bronchiectasis.

Stages of Clubbing

- Early sign: Increased sponginess of proximal nail bed (fluctuation is positive). This is due to increased proliferation of cells at nail base.
- Swelling of subcutaneous tissue in nail base leading to shiny, red colouration and obliteration of skin creases.
- Increased curvature of nails. Hence nails become convex, and the angle between the nail and its base is obliterated.
- Later, drumstick appearance.
- Lastly, parrot-beak appearance.
- Hypertrophic osteoarthropathy may occur.

Q: What are the pathogeneses or mechanisms of clubbing?
A: Actual mechanism is unknown. But there are possible hypotheses:

- Arterial hypoxaemia.
- Humoral substances that cause vasodilatation (bradykinin, prostaglandins, 5-hydroxytryptamine).
- Neurogenic factors through vagal stimulation (vagotomy revert clubbing in some cases).
- Platelet-derived growth factor (PDGF) released from megakaryocyte and platelet emboli in nail bed is thought to be a probable factor, which causes increased capillary permeability, fibroblastic activity and arterial smooth muscle hyperplasia in the nails resulting in clubbing.
- Tumour necrosis factor has been implicated.



Thyroid acropachy in both hands



Clubbing with cyanosis

Q: What is **thyroid acropachy**?

A: If hyperthyroidism is associated with clubbing, diffuse thickening of distal extremity and subperiosteal new bone formation of hands and feet, it is called **thyroid acropachy**.

- Usually involves metacarpals and phalanges.
- Long bones are rarely involved.
- Usually associated with exophthalmos.
- Thyroid acropachy is present only in Graves disease.

Q: If there is clubbing, can it be **reversible** by any therapy?

A: Yes, clubbing may be reversible, rarely, if vagotomy is done (in idiopathic or sometimes familial clubbing).

Q: What **history** should be taken in clubbing?

A: As follows:

- Family history.
- Respiratory problem such as cough, haemoptysis, chest pain, breathlessness.
- Cardiac: History of cyanotic congenital heart disease.
- Gastrointestinal tract (GIT): Diarrhoea, blood in the stool.
- History of liver disease.

Q: What **investigations** should be done in clubbing?

A: As follows:

- Full blood count.
- Chest X-ray.
- Ultrasonography (USG) of whole abdomen.
- Echocardiography.
- Other, according to suspicion of cause (barium enema, follow through, colonoscopy, etc. for inflammatory bowel disease, liver function test, etc.).

Hypertrophic Osteoarthropathy

- Hypertrophic osteoarthropathy (HOA) is the **triad** of clubbing, arthritis and subperiosteal new bone formation (periosteal inflammation at the distal ends of long bones in radius, ulna, tibia, fibula; although any bone may be involved).
- There is swelling and tenderness at the lower ends of forearm and leg. Clubbing is usual, but not invariable in HOA (rarely occur without HOA).
- HOA may be primary or secondary to any cause of clubbing.
- The commonest causes of HOA are bronchial carcinoma (squamous cell type) and pleural mesothelioma.
- Mechanism and pathogenesis of HOA are same as clubbing.



Thyroid acropachy



Pachydermoperiostosis

Primary hypertrophic osteoarthropathy:

- It is also called pachydermoperiostosis.
- Usually begins in childhood or puberty, inherited as autosomal dominant, more in male.
- There is thickening of the skin of face and scalp, which is greasy, pigmented, furrowed forehead giving rise to 'Leonine facies'. Also, increased sweating especially of palm and sole.
- Usually marked clubbing is present and distal extremities are large and thick, giving rise to elephant feet (very large feet, confuses with mucopolysaccharidoses).

Koilonychia

Usual instructions are:

- Perform the general examination.
- Look at the nail. What is your diagnosis?

Presentation of a Case

- The patient is severely anaemic.
- There is koilonychia involving all the nails of fingers and toes.
- Tongue is smooth and shiny with atrophy of papillae.

Diagnosis is **severe anaemia with koilonychia** (due to iron-deficiency anaemia).

Q: What are the **causes** of koilonychia?

A: As follows:

1. Iron-deficiency anaemia (the commonest cause).
2. Others (rare, **better do not mention** until asked)
 - Trauma (rarely in garage mechanics, who regularly fit tyres).
 - Thyrotoxicosis.
 - Fungal infection.
 - Raynaud disease.

Q: What is **koilonychia**?

A: A disorder in which nail is concave or spoon shaped.

Q: What is the **mechanism** of koilonychia?

A: Unknown, probably results from slow growth of nail plate.



Koilonychia



Pallor of palm

Q: What are the **stages** of koilonychia?

A: As follows:

- Dryness, brittleness and ridging (first stage).
- Flattening and thinning (second stage).
- Spooning or concavity (third stage).

Q: **What else** do you want to ask or see? **Why?**

A: I want to take history of dysphagia. Also, I want to look at the tongue to see evidence of glossitis.

Presence of these two findings associated with koilonychias is suggestive of **Plummer–Vinson** syndrome.

Q: What is **Plummer–Vinson** syndrome? What are the features? How to treat?

A: It is the combination of:

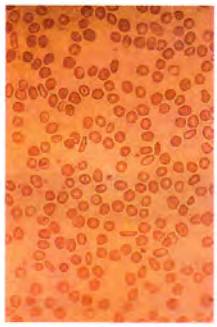
- Iron-deficiency anaemia.
- Dysphagia (due to postcricoid web secondary to epithelial degeneration).
- Glossitis.

It is also called Paterson–Brown–Kelly syndrome, common in women; its cause is unknown. There is constriction in upper oesophageal sphincter in the postcricoid region and appears radiologically as a web. This web may be asymptomatic or may produce dysphagia. It may be difficult to see endoscopically. Rarely, there is increased risk of squamous cell carcinoma.

Treatment: Iron therapy. Rarely, dilatation may be required. If severe anaemia, blood transfusion should be given.



Glossitis with angular stomatitis in iron-deficiency anaemia



Pencil cells, target cells, microcytosis, hypochromia in iron-deficiency anaemia

Nail Changes in Different Diseases

Instruction to the examinee:

- Examine the hands of this patient.
- Look at the nail. What is your diagnosis?

Presentation of a Case (Supposing White Nail)

- All the nails of the toes of toes and fingers are white.

My diagnosis is **leukonychia**.

Q: What does leukonychia indicate?

A: It indicates hypoalbuminaemia. However, it may be physiologically normal.

Q: Which organ is involved?

A: Liver, kidney, GIT; also, less intake of food.

Q: What is leukonychia? What are the causes?

A: It means white nail. It may be diffuse, punctate, linear or striate (white transverse flecks—a normal finding). Causes are:

- Renal cause [nephrotic syndrome, chronic renal failure (CRF)].
- Liver diseases [chronic liver disease (CLD), cirrhosis of liver].
- Malnutrition (malabsorption, less intake of food).
- May be normal finding in some cases.
- Others: Rare (lymphoma, fungal infection, congenital).
- Striate leuconychia (a normal finding due to minor trauma).

Mechanism of leuconychia is unknown; it may be due to compression of capillary flow by extracellular fluid.



Leuconychia



Nail fold infarction



Splinter haemorrhage

Q: How will you investigate leukonychia?

A: I will take the history of the patient. Investigation should be done according to the history and physical finding such as:

- If history is suggestive of CLD: I will do liver function test.
- If history is suggestive of renal disease: I will investigate accordingly.
- If history is suggestive of GIT: I will investigate accordingly.

Q: What **diseases** are diagnosed by examining the nail?

A: Nail abnormality may occur in many local, systemic and dermatological diseases. Hence, these should be examined carefully. A good visual impression is very essential and a spot diagnosis can be done easily. These are described below.

Clubbing, koilonychias, leukonychia: Already described.

Pale nail: Found in anaemia.

Nail fold infarction: Causes are (usually vasculitis due to any cause):

- SLE.
- Dermatomyositis.
- Systemic sclerosis.
- Rheumatoid arthritis (RA).
- Polyarteritis nodosa.

Splinter haemorrhage: Linear dark brown, longitudinal flecks, parallel to long axis of nail. Causes are:

- Trauma (the commonest).
- SBE.
- Septicaemia.
- Collagen disease (vasculitis): SLE, RA and polyarteritis nodosa.
- Others: Haematological malignancy, severe anaemia, psoriasis. Rarely in trichinosis (usually transverse haemorrhage).

Half-and-half nail: Proximal part of nail is white-to-pink and distal part is red or brown. Causes are:

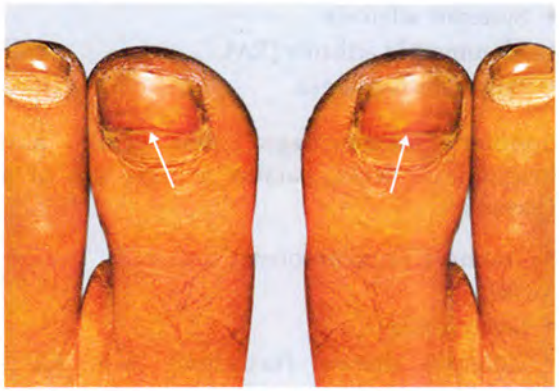
- CRF (the commonest cause).
- Cirrhosis of liver.
- Occasionally, in normal person.
- Red half moon occurs in congestive cardiac failure (CCF).



Half-and-half nail



Nail fold telangiectasia



Beau line



Onycholysis/fungal nail

Nail fold telangiectasia: Causes are:

- SLE.
- Systemic sclerosis.
- Dermatomyositis.
- Mixed connective tissue disease (MCTD).
- Raynaud phenomenon.

Beau line: Nonpigmented transverse line or grooves in nail due to transient arrest of nail growth. This appears at the same time, on all the nails, a few weeks after an acute illness. Causes are:

- Chronic illness (chronic infection, malignancy and collagen disease).
- Prolonged fever.
- Pneumonia.
- Coronary artery disease.
- Others: Cachexia, malnutrition, psychiatric illness, use of cytotoxic drugs.

Onycholysis: Separation of distal nail plate from the nail bed (free edge looks white). Causes are:

- Psoriasis (the commonest).
- Fungal infection.
- Thyrotoxicosis (Plummer sign).
- Idiopathic.
- Occasionally drugs (tetracycline and psoralen).
- Porphyria.
- Trauma or faulty manicure.

Mee line: Single transverse white band in nail. Causes are:

- Chronic arsenic poisoning.
- CRF.
- Also, after chemotherapy and severe illness.



Mee line



Yellow nail

Yellow nail: Found in yellow nail syndrome, an inherited disease in which the nails are thick, yellow or pigmented with separation of distal part of nail bed due to hypoplasia of lymphatic system. It is associated with lymphoedema of legs, bronchiectasis and pleural effusion.

Loss of nail (or dystrophy): Causes are:

- Severe lichen planus.
- Epidermolysis bullosa.
- Trauma (tooth biting).

Nail pitting (depression in nail): Causes are:

- Psoriasis.
- Alopecia areata.

- Atopic eczema (when involves proximal nail bed).
- Pityriasis rosacea.

Brittle nail (easily broken): Causes are:

- Iron-deficiency anaemia.
- Peripheral vascular disease.
- Fungal infection.
- Hypocalcaemia.
- Psoriasis.
- Injury (nail biting).
- Idiopathic.

Blue nail: Normal white lunulae become blue, found in Wilson disease due to deposition of copper (normally, half-moon lunulae at the proximal end of nail is white-blue half moon). Also found in cyanosis and ochronosis.



Fungal nail



Hypoplastic nail

Red nail: May be normal finding. Also in polycythaemia, carbon monoxide poisoning (cherry red).

Brown nail: Usually present in chronic kidney disease (CKD).

Periungual or subungual fibroma: Suggests tuberous sclerosis (epiloia).

Fungal nail: Nail has thick, white, green, black, discolouration and crust formation.

Absent or small, dysplastic nail: Its causes are:

- Nail patella syndrome [autosomal dominant (AD), associated with no or hypoplastic patella and glomerulonephritis, abnormalities in eye].
- Others: Congenital, traumatic and vasculitis.

Nail hyperpigmentation: May occur due to some drugs (such as zidovudine, doxorubicin, bleomycin, cyclophosphamide, fluorouracil, melphalan and nitrosoureas).

Terry nail: Proximal part is white or pink, but nail tip is red or brown. It is due to decrease in vascularity and an increase in connective tissue within the nail bed. Causes are:

- Old age (normally present in elderly).
- Cirrhosis of liver.
- CCF.
- Hyperthyroidism.
- Malnutrition.
- Renal failure.

Dark nail: May be a normal finding, mostly in black people. Sometimes may be due to subungual melanoma.

N.B. Remember the following points:

- Normal nail growth is 0.1 mm/day; finger nails grow quickly than toe nails.
- Nail plate grows continuously and slowly at the rate of 1 cm every 3 months. Hence, renewal of finger nails take about **3–6 months,** and **toe nails** that grow more slowly take **1 year**.
- Rapid growth of nail plate occurs in psoriasis.
- Nail growth is arrested by acute illness and ischaemia (Beau line).





Periungual fibroma

Cervical Lymphadenopathy

The usual instructions are:

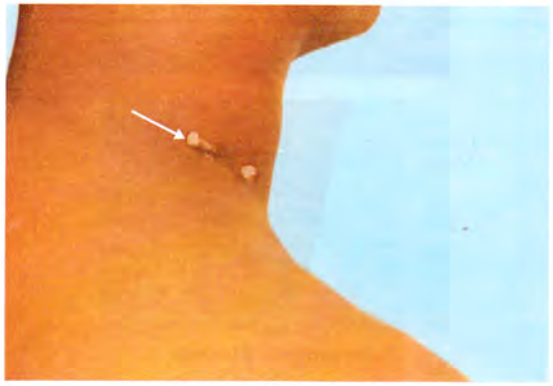
- Perform the general examination or examine the neck.

Once lymph node (LN) is palpable, examine the following points:

- Site (anterior or posterior chain, supraclavicular, submental or submandibular in right or left or both sides).
- Number (single or multiple).
- Size (large LN is abnormal, >1 cm is pathological. Size 2 × 2 cm may be suggestive of neoplastic lesion).
- Consistency (soft or firm, or rubbery or hard).
- Tenderness (suggests acute inflammation).
- Discrete or matted (matted in TB).
- Fixation (to underlying structure or overlying skin suggests malignancy).
- Skin (sinus, ulcer and signs of acute inflammation). Tethering of skin suggests malignancy. Note for scar mark (biopsy), if any.



Cervical lymphadenopathy



Tuberculous sinus



Cervical lymphadenopathy (scar mark seen)

Presentation of a Case

- There is cervical lymphadenopathy involving the anterior chain in right or left side (mention the position).
- LNs are of variable size and shape and firm in consistency; some are matted, nontender and free from the underlying structure and the overlying skin.

Q: What are the causes of cervical lymphadenopathy?

A: According to the characteristics of the lymph nodes of that patient, mention the common causes as follows:

If matted cervical lymphadenopathy, the causes are:

- Tuberculous lymphadenitis (the commonest).
- Infection by atypical mycobacteria.
- Actinomycosis.
- Sometimes, lymphoma (in advanced stage), metastasis.

If lymphadenopathy with sinus, the causes are:

- Tuberculous lymphadenitis.
- Actinomycosis.

If lymphadenopathy with biopsy marking, the causes are:

- Tuberculosis.
- Lymphoma.
- Secondaries.

If hard lymphadenopathy, the causes are:

- Metastatic malignancy (e.g. from bronchial carcinoma).

If tender cervical lymphadenopathy, the causes are:

- Acute inflammation (may be secondary to dental sepsis, tonsillitis and mastoiditis).
- Infection of LNs itself.

If lymphadenopathy is discrete, the causes are:

- Lymphoma.
- Infectious mononucleosis.
- Reactive hyperplasia.

If lymphadenopathy with goitre, the cause is:

- Papillary carcinoma of thyroid with metastasis.

If lymphadenopathy is soft, fleshy, rubbery and discrete, the cause is:

- Lymphoma.

If lymphadenopathy is immobile, fixed to skin, the cause is:

- Metastatic malignancy.

Q: In which disease, biopsy should not be done?

A: Leukaemia. (With biopsy marking, leukaemia is unlikely. Leukaemia is diagnosed by blood and bone marrow examination. Biopsy is not done in leukaemia, rather it is contraindicated.)

Consistency of LNs suggests the following, if:

- Rubbery: Lymphoma.
- Firm and matted: TB.
- Hard and craggy: Malignancy.
- Stony hard: Calcified LN.
- Soft, cystic: Cold abscess.

Q: What investigations are done in tuberculous lymphadenitis?

A: As follows:

- Complete blood count (CBC) and erythrocyte sedimentation rate (ESR) (high).
- Chest X-ray, posterior–anterior (PA) view (to see TB in chest).
- Tuberculin test.
- For confirmation, perform fine needle aspiration cytology (FNAC) or biopsy [for histology, acid-fast bacillus (AFB), mycobacterial culture and sensitivity (C/S)].

FNAC or biopsy of LN in TB shows the following:

- In 50% cases, AFB is positive.
- In 70–80% cases mycobacterial C/S is positive.
- Granuloma is present in most cases.

Q: How to treat tuberculous lymphadenitis?

A: With standard anti-Koch for 9 months to 1 year.

N.B. Following anti-TB drug therapy, the LNs may be enlarged. It is due to hypersensitivity reaction to tuberculoprotein, released from dead mycobacteria.

Q: What are the atypical mycobacteria?

A: Atypical mycobacteria, also called nontuberculous mycobacteria (NTM) or mycobacteria other than TB (MOTT). The following are atypical mycobacteria:

- *Mycobacterium scrofulaceum*
- *Mycobacterium avium* intracellulare complex (MAC)
- *Mycobacterium kansasii*
- *Mycobacterium bovis*
- *Mycobacterium xenopi*
- *Mycobacterium chelonei*
- *Mycobacterium malmoense*
- *Mycobacterium marinum*
- *Mycobacterium fortuitum*

Atypical mycobacteria commonly affect the children. It may also cause disseminated infection in HIV, pulmonary infection (by MAC).

Q: How to treat atypical mycobacteria?

A: If there is localised involvement in cervical LN, perform surgical excision. Most organisms are resistant to standard anti-TB drug.

Drugs used are the combination of:

- Clarithromycin 500 mg twice daily or azithromycin 500 mg daily **plus**
- Ethambutol 15 mg/kg **plus**
- Rifabutin 300 mg daily.

However, standard anti-TB therapy with rifampicin, ethambutol, isoniazid (INH) and pyrazinamide are commonly used. Injection streptomycin is also effective.

N.B. Remember, if no response, there is possibility of MDR–TB.

Causes of localised lymphadenopathy in different sites

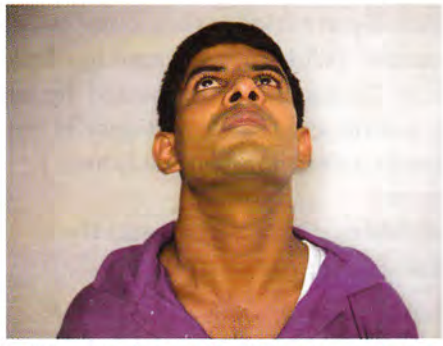
1. Epitrochlear: This is always pathological. Its causes are:
 - Localised infection in hand or arm (the commonest cause).
 - Lymphoma (usually non-Hodgkin).
 - Sarcoidosis.
 - Secondary syphilis.
 - Tularaemia.
2. Unilateral axillary lymphadenopathy: Its causes are:
 - Local infection in upper extremity.
 - Carcinoma of breast with metastasis.
 - Lymphoma (non-Hodgkin commonly).
 - Brucellosis.
 - Cat-scratch disease.
3. Scalene LNs involvement: Its causes are:
 - Lymphoma.
 - Metastasis from carcinoma of bronchus.
 - Sarcoidosis.
 - TB.

N.B. Remember the following points:

1. If only left supraclavicular LN is palpable, it is called Troisier sign. Then palpate abdomen to see any epigastric mass carcinoma of stomach.
2. For a particular area of lymphadenopathy, examine the drainage area:
 - Cervical lymphadenopathy (examine the mouth, tonsil, teeth, face, ears and scalp).
 - Axillary lymphadenopathy (examine the breasts, chest and upper limbs). Supraclavicular lymphadenopathy (examine the chest for bronchial carcinoma).
 - Left supraclavicular lymphadenopathy or Virchow gland (palpate for epigastric mass, carcinoma of stomach).
 - Inguinal lymphadenopathy (examine the lower limbs for any septic focus, genitalia and perineum).



Cervical lymphadenopathy (lymphoma; side view)



Cervical lymphadenopathy (lymphoma; front view)

Generalised Lymphadenopathy

Examine systematically starting from the neck, axilla, inguinal and para-aortic.

Presentation of a Case

- There is generalised lymphadenopathy involving cervical, supraclavicular, axillary and inguinal.
- LNs are of variable size and shape, firm in consistency; some are rubbery, discrete, nontender, and free from underlying structure and overlying skin.

Q: What relevant do you like to see?

A: As follows:

- LNs in other parts (axillary, inguinal, para-aortic, when asked to examine the neck only).
- Liver and spleen (lymphoma and leukaemia).
- Anaemia and bony tenderness (leukaemia).
- Purpura or bruise or petechiae (haematological malignancy).
- Palatal petechial haemorrhage (infectious mononucleosis and leukaemia).
- Cachexia (disseminated TB or secondaries).

Q: What are the causes of generalised lymphadenopathy?

A: (Mention the common causes of that patient, considering the age)

If the patient is young or child, the causes are:

- Lymphoma (usually Hodgkin).
- Acute lymphoblastic leukaemia (ALL).
- Viral infection (infectious mononucleosis and cytomegalovirus infection).
- Others: Disseminated TB and SLE.

If the patient is middle-aged or elderly, the causes are:

- Lymphoma.
- Chronic lymphatic leukaemia (CLL).
- Viral infection (infectious mononucleosis and cytomegalovirus infection).
- Disseminated TB.
- Others: Sarcoidosis, brucellosis, toxoplasmosis and HIV.

Q: What are the causes of **generalized lymphadenopathy? (theoretically).**

A: As follows:

1. Haematological malignancy: Lymphoma, acute lymphoblastic leukaemia (ALL), chronic lymphocytic leukaemia (CLL).
2. Viral fever: Infectious mononucleosis, cytomegalovirus (CMV) infection, human immunodeficiency virus (HIV).
3. Other infections: Disseminated tuberculosis, brucellosis, toxoplasmosis.
4. Sarcoidosis.
5. SLE.
6. Drugs: Phenytoin or diphenylhydantoin (called pseudolymphoma).

Q: If the patient has **generalized lymphadenopathy with arthritis,** what are the likely causes?

A: As follows:

- Juvenile idiopathic arthritis (JIA) (early age).
- SLE.
- Sarcoidosis.
- Viral-fever-like infectious mononucleosis, CMV infection.
- Brucellosis.

Q: What are the **causes of lymphadenopathy with splenomegaly** (and/or hepatomegaly)?

A: As follows:

- Lymphoma.
- ALL or CLL.
- Infectious mononucleosis.
- SLE.
- Sarcoidosis, brucellosis and toxoplasmosis.
- HIV.

Q: What are the causes of generalized lymphadenopathy with fever?

A: As follows:

- Lymphoma.
- ALL and CLL.
- Viral infections (e.g. infectious mononucleosis, CMV infection).
- Disseminated tuberculosis.
- Brucellosis.
- Sarcoidosis.
- Toxoplasmosis.

Q: What **investigations** do you suggest in generalised lymphadenopathy?

A: As follows:

1. CBC, erythrocytic sedimentation rate (ESR) and peripheral blood film (PBF) (to exclude leukaemia, increase of eosinophil in lymphoma, atypical lymphocyte in infectious mononucleosis and high ESR in TB).
2. Chest X-ray (to see evidence of TB, bilateral hilar lymphadenopathy (BHL) in lymphoma and lymphatic leukaemia).
3. Ultrasonography or CT scan of abdomen (to see hepatomegaly, splenomegaly, para-aortic and other lymphadenopathy).
4. Others according to the suspicion of cause:
 - If lymphoma is suspected: FNAC or biopsy (biopsy is preferable) of lymph nodes.
 - If leukaemia is suspected: Bone marrow study.
 - If disseminated tuberculosis: Mantoux test (MT), lymph node FNAC or biopsy.
 - If HIV is suspected: HIV screening test.
 - If SLE: Antinuclear antibody (ANA), anti-double stranded DNA (anti-ds-DNA), etc.

Q: If a patient presents with generalized lymphadenopathy, how will you **proceed** to diagnose?

A: As follows:

1. Detailed history of the patient: Fever, loss of weight, sweating, itching,
2. Physical examination: Detailed findings of lymph node (e.g. site, size, consistency, tenderness, overlying skin and underlying structure, any sinus, etc). Also, hepatosplenomegaly, skin rash, joints, etc.
3. Investigation (as above).

N.B. Remember the following points:

- Normal LNs may be palpable in axilla, groin, usually up to 0.5 cm, which are soft, rubbery, shotty. Submandibular LNs <1 cm is normal in children and inguinal LNs <2 cm is normal in adult.
- Reactive LNs expand rapidly and may be painful.
- Localised lymphadenopathy means single anatomical area of LN involvement.
- Generalised lymphadenopathy means three or more anatomical noncontiguous areas of LN involvement.
- Enlargement of supraclavicular and scalene LNs are always pathological.

Lymphoreticular System

Lymphoreticular system includes LNs, spleen, tonsil, adenoid, Peyer patch of ileum and Kupffer cells in liver.

Groups of cervical LNs:

- Submental.
- Submandibular.
- Anterior cervical (in front of the anterior border of the sternomastoid).
- Posterior cervical (behind the posterior border of the sternomastoid).
- Supraclavicular.
- Preauricular.
- Postauricular.
- Suboccipital.

Five groups of axillary LNs:

- Anterior.
- Posterior.
- Lateral.
- Central.
- Apical.



Generalised lymphadenopathy

Pigmentation

Usual instructions:

- Perform the general examination.
- Look at the patient. What do you think? (Pigmentation may be found).

Once there is pigmentation, look carefully at the following points:

- Generalised or localised.
- Lips, gum, inner side of mouth or buccal mucosa, and tongue.
- Exposed parts (face, neck and extensors of arm).
- Palm (especially the creases).
- Pressure areas (knee or elbow).
- Scars (especially recent).
- Nipples.
- Genitalia.

Presentation of a Case

- There is generalised (or localised) pigmentation involving gums, buccal mucosa, tongue and other parts of skin (mention the location).
- Vitiligo is present (describe, if any).

Q: What do you think are the causes in this case?

A: (Mention about the causes of that patient):

- Kala-azar (history of fever).
- Addison disease.
- Haemochromatosis or primary biliary cirrhosis (PBC).
- Drugs (busulphan, amiodarone and phenothiazine).
- Chronic debilitating illness (malignancy, CRF and TB).
- Chronic arsenic toxicity.
- Malabsorption syndrome (Whipple disease).



Generalised pigmentation (haemochromatosis)



Generalised pigmentation (systemic sclerosis)



Generalised pigmentation



Addison disease

Q: How to **investigate** a patient with pigmentation?

A: As follows:

1. History of fever (such as kala-azar).
2. History of drugs.
3. History suggestive of chronic disease (CLD and CRF) and Addison disease.
4. Physical examinations:
 - BP (low in Addison disease).
 - Hepatosplenomegaly (kala-azar).
 - Signs of CLD or haemochromatosis or PBC.
 - Abdomen (scar of bilateral adrenalectomy in Nelson syndrome).
 - Evidence of other chronic illness.
5. Laboratory investigations: According to the history and suspicion of causes (kala-azar, Addison disease and haemochromatosis).

Q: Why **drug** causes pigmentation?

A: This is due to melanocyte stimulation or deposition of drug in the skin.

Q: What are the **causes** of localised pigmentation?

A: Any cause of generalised pigmentation may be manifested as localised pigmentation initially. The other causes are:

- Local radiation therapy, friction or scratching.
- Melasma.
- Erythema ab igne (see page 23).

Q: What is **Peutz–Jeghers** syndrome?

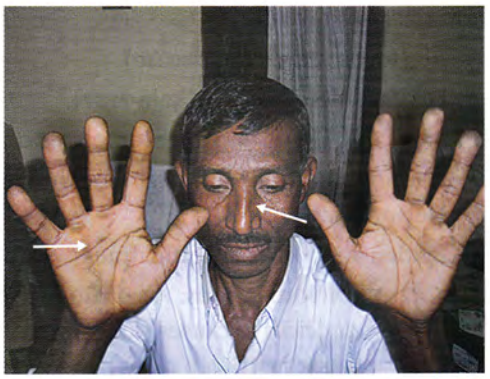
A: It is a disorder inherited as autosomal dominant, characterised by mucocutaneous pigmentation in the lips, around the mouth, eyes, nose, buccal mucosa (never tongue), hands and feet, associated with polyp in GIT.

Polyp is usually hamartomatous, benign, involves any part of GIT, commonly small bowel. It may cause bleeding, recurrent abdominal pain, intestinal obstruction and intussusception. Almost never or very rarely it turns to malignancy.

Treatment involves polypectomy. Small bowel resection is usually avoided (polyp may recur).



Perioral pigmentation in Peutz–Jeghers syndrome



Pigmentation in palmar crease and face (Addison disease)



Ochronosis (ear pigmentation)

Causes of pigmentation

A. **Physiological** (familial, racial, pregnancy and sun bath).

B. **Pathological:**

1. Endocrine causes
 - Addison disease (brown or dark brown).
 - Cushing syndrome.
 - Acromegaly.
 - Nelson syndrome (bilateral adrenalectomy, look for abdominal scar, visual field defect).
 - Thyrotoxicosis.
2. Infections (kala-azar and TB).
3. CLD:
 - Haemochromatosis (greenish or bronze, less involvement of mucous membrane).
 - Cirrhosis of liver (common in PBC).
4. GIT malabsorption syndrome (Whipple disease, Peutz–Jeghers syndrome).
5. Chronic debilitating illness:
 - Internal malignancy [commonly ectopic adrenocorticotropic hormone (ACTH) syndrome].
 - CRF.
 - Any chronic illness.
6. Drugs:
 - Busulphan.
 - Bleomycin (diffuse brown).
 - Amiodarone (violaceous or brown or blue or slaty-grey, in exposed parts).
 - Phenothiazine (slaty-grey).
 - Phenytoin (melasma-like pigmentation).
 - Adrenocorticotropic hormone.
 - Oral contraceptive pill.
 - Chloroquine (blue–grey).
 - Clofazimine (red or pinkish).
 - Psoralen (brown).
 - Minocycline.
 - Other cytotoxic drugs.
7. Others:
 - Chronic arsenic poisoning.
 - Pellagra (necklace area and exposed part).
 - Systemic sclerosis.
 - Ochronosis (mainly in the joint, nose, ear and face).
 - Argyria (slaty grey hue due to silver deposition).
 - Porphyria cutanea tarda.
 - Acanthosis nigricans.

Erythema Ab Igne

The usual instructions are:

- Look here. What is the diagnosis?

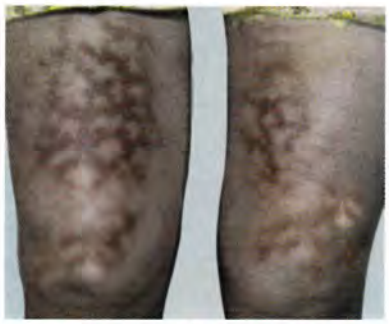
Presentation of a Case

- There is reticular pattern of pigmentation involving (mention the location).

Diagnosis is erythema ab igne.

Q: What is the probable underlying disease? What history do you like to take?

A: Hypothyroidism or severe pain. History of application of hot water bag or bottle to relieve pain or to relieve from cold.



Erythema ab igne (legs)

Q: What is **erythema ab igne**? What are the **causes**?

A: It is characterised by reticular pattern of pigmentation that occurs due to prolonged exposure to excessive heat without production of burn. It is due to repeated infrared heat injury. Occurs on any part of the body, where heat is applied. Histology shows increased amount of elastic tissue in dermis. Its **causes** are:

- Those who sit near the fire or those who use hot water bottle on belly or thigh or on back due to severe pain.
- Hypothyroidism (patient applies hot because of coldness).

Treatment of erythema ab igne:

- 0.1% retinoic acid with 0.1% dexamethasone cream applied locally.
- 5% hydroquinone applied locally.

Complications of erythema ab igne: In long-standing cases, premalignant keratosis and squamous cell carcinoma.

Differential diagnosis of reticular pattern of pigmentation:

- Erythema ab igne.
- Livedo reticularis.
- Cutis marmorata (a physiological reaction to cold in children and adult).



Erythema ab igne (abdomen)

Gynaecomastia

The usual instructions are:

- Perform the general examination.
- Look at the chest. What is your finding? What else do you want to examine?

Proceed as follows:

- Look at the chest (unilateral or bilateral breast enlargement).
- Palpate the glandular tissue, first with palm, then with fingers (to differentiate from *lipomastia in obese*).
- Tender or nontender.
- Any secretion.

Presentation of a Case

- There is gynaecomastia, right or left or bilateral, tender (or nontender). Right or left is larger.

Q: What **else** or **relevants** do you want to examine to find out causes?

A: As follows:

- Age (in young, puberty gynaecomastia).
- History of taking drugs (spironolactone, digoxin, cimetidine and oestrogen).
- Signs of CLD.
- Bronchial carcinoma (in the elderly) with cachexia, clubbing with nicotine staining, radiation mark in chest.
- Body habitus (tall and obese, small testes, absent or less secondary sex characters in Klinefelter syndrome).
- Palpate the testes (to see atrophy, tumour or ambiguous genitalia).
- Endocrine abnormality (hypopituitarism, thyrotoxicosis and Addison disease).

Q: What do you think are the **causes**?

A: Describe the causes according to age of the patient.

If the patient is young, the causes are:

- Puberty (normal physiological).
- Drugs (spironolactone, digoxin, cimetidine and INH).
- Testicular tumour (teratoma and Leydig cell tumour).
- Secondary testicular failure (trauma, orchidectomy and leprosy).
- CLD (due to Wilson disease and alpha-1-antitrypsin deficiency).

If the patient is elderly or middle-aged, the causes are:

- Drugs (as above, also oestrogen therapy for carcinoma of prostate).
- Bronchial carcinoma.
- Chronic liver disease.
- Testicular tumour.
- Secondary testicular failure (trauma, orchidectomy and leprosy).

Q: How to differentiate gynaecomastia from lipomastia?

A: As follows:

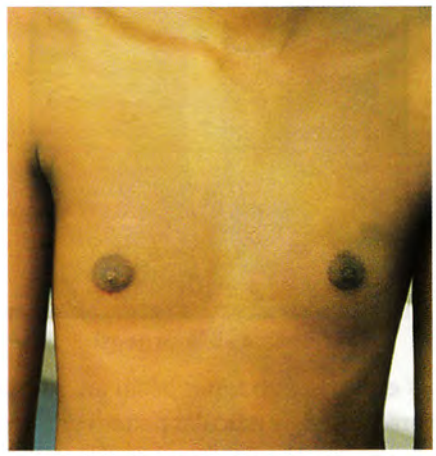
- Lipomastia is due to deposition of fat in the breast. Therefore, it is soft.
- Gynaecomastia is the enlargement of male breast due to glandular tissue proliferation. Hence, it is firm, hard or rubbery.

N.B. Remember the following points:

- Unilateral gynaecomastia in the elderly is highly suspicious of malignancy (hard, fixed to underlying tissue, associated with skin tethering and nipple discharge).
- Carcinoma of breast is 16 times common in Klinefelter syndrome.



Unilateral gynaecomastia (left)



Lipomastia with striae in Cushing syndrome



Bilateral gynaecomastia



Lipomastia

Q: What are the mechanisms of gynaecomastia?

A: The four possible mechanisms are:

1. Increased oestrogen, and its causes are:
 - CLD.
 - Bronchial carcinoma [due to increased human chorionic gonadotropin (HCG) production].
 - Leydig cell tumour of the testis (due to increased oestrogen).

- Adrenal carcinoma and congenital adrenal hyperplasia.
- Thyrotoxicosis (due to increased conversion of oestrogen from androgen).
- Starvation (due to disturbance of liver function).

2. Reduction of circulating androgens:
 - Klinefelter syndrome.
 - Primary and secondary hypogonadism.
 - Testicular failure (orchitis, trauma, surgery and radiation).
3. Antagonism of androgen action (using spironolactone and cimetidine).
4. Androgen-resistant state or insufficiency (in testicular feminisation syndrome).

Q: What is **gynaecomastia**? What are the causes?

A: Enlargement of male breast due to proliferation of glandular components. It is due to disturbance of normal ratio of active androgen to oestrogen in plasma or breast (normal ratio of testosterone:oestrogen is 100:1 and normal ratio of these in blood is 300:1).

Imbalance occurs either due to less testosterone production or action or increased oestrogen synthesis or both.

Causes of gynaecomastia:

A. Physiological

1. Pubertal (50% cases) may be unilateral due to transient increase in oestradiol level. Resolves spontaneously in 6–18 months.
2. Senile (40% or more) due to increased oestrogen from conversion of androgen to oestrogen (also decline of Leydig cell in testis).
3. Newborn (due to transplacental transfer of maternal oestrogen).

B. Pathological

1. CLD (common in alcoholic liver disease), hepatocellular carcinoma (HCC) (HCG-secreting).
2. Bronchial carcinoma (5% case, HCG-secreting).
3. Hypogonadism:
 - Primary testicular diseases (testicular tumour, teratoma and Leydig cell tumour).
 - Testicular failure (trauma, orchidectomy, radiation and leprosy, TB, mumps orchitis, haemochromatosis and Klinefelter syndrome).
 - Secondary testicular failure (hypopituitarism, hyperprolactinaemia, Kallman syndrome).
4. Endocrine disease (acromegaly, thyrotoxicosis, hypothyroidism, adrenal carcinoma, Addison disease).
5. Drugs (spironolactone, digoxin, cimetidine, INH, oestrogen therapy for prostate carcinoma, alcohol, alkylating agent, methyldopa, marijuana, amiodarone).
6. Chromosomal abnormalities: Klinefelter syndrome, Kallman syndrome [anosmia, cryptorchidism, small testis, cleft lip or palate, low gonadotrophin-releasing hormone (GnRH), hence low luteinizing hormone (LH) and follicle stimulating hormone (FSH), low testosterone].
7. Others: Testicular feminisation syndrome, starvation and idiopathic.

Q: What are the causes of **painful gynaecomastia**?

A: As follows:

- Puberty.
- Drugs (spironolactone and cimetidine).
- Chronic liver disease.

Q: Why **gynaecomastia in CLD**?

A: Probable mechanisms are:

- Excess oestrogen due to increased conversion from androgens and altered oestrogen metabolism by liver.
- Drug (spironolactone therapy for ascites).

Q: Why **alcohol** causes gynaecomastia?

A: Alcohol may cause gynaecomastia by causing CLD or by damaging Leydig cells of testis without CLD.

Q: How will you **investigate** a case of gynaecomastia?

A: Depending on the age. If the patient is young, it may be due to puberty. No need of further investigation. Otherwise as follows:

1. History of drug intake.
2. Chest X-ray (to exclude bronchial carcinoma).
3. Liver function tests (in CLD).
4. Endocrine evaluation:
 - In hypogonadism, serum testosterone, LH, FSH, oestradiol, prolactin and HCG should be estimated.
 - If LH and FSH are high, but testosterone is low, then the cause is primary testicular failure.
 - If both LH and testosterone are low, the cause is increased oestrogen production from tumour of testis.
 - If both LH and testosterone are high, there is androgen-resistant state or gonadotrophin-secreting tumour.
 - 24 h urinary 17-ketosteroid or serum and androstenedione should be done.

- If plasma β-HCG (human chorionic gonadotrophin) is increased, it indicates testicular tumour. It is also increased in bronchial carcinoma.

5. Other investigations: According to suspicion of causes (chromosomal analysis in Klinefelter syndrome).

Q: How will you **treat** gynaecomastia?

A: As follows:

- Explanation and reassurance to the patient, especially in younger age. Usually improve or disappears spontaneously.
- Treatment of primary cause. If any offending drug is responsible, it should be stopped.
- If severe and progressive or suspicion of malignancy, mastectomy should be done.

Erythema Nodosum

The usual instructions are:

- Look at the leg. What is your finding? What else do you want to examine?

Look carefully the following points (look and feel):

- Swelling (multiple, nodular, variable in size and shape).
- Colour (red-to-bluish or pigmented).
- Palpate (Tender nodule: Look at the face, patient winces, if pain).

Presentation of a Case

- There are multiple nodular, tender lesions of variable size and shape; some are red and some are pigmented in the right or left or both shins.

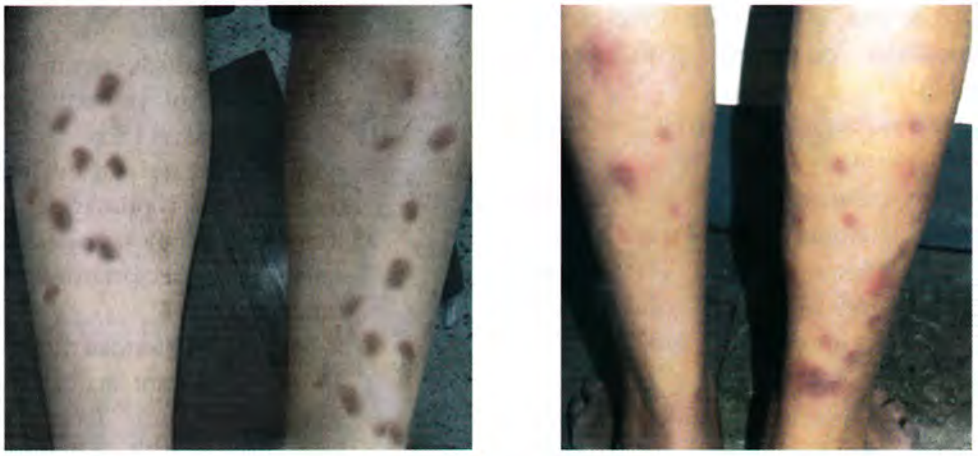
Differential diagnosis includes:

- Drug rash.
- Erythema nodosum.
- Erythema multiforme.
- Purpura.
- Cellulitis.
- Erythema induratum.
- Others: Nodular panniculitis, meningococcal septicaemia, vasculitis [SLE and polyarteritis nodosa (PAN)].

Q: What is **erythema nodosum**? What are the **histological findings**?

A: It is characterised by nonsuppurative, painful, palpable, erythematous nodular lesion in the skin due to vasculitis in dermis and subcutaneous fat. Usually, it is associated with fever and arthralgia, and is common in shin below the knee. Nodules may be 2–6 cm in diameter, occur in crops, over 2 weeks, then resolve slowly over months leaving a bruise staining in the skin. It never ulcerates, may be recurrent and common in adult female.

Microscopy: Panniculitis (inflammatory reaction in fat), infiltration of lymphocytes, histiocytes, multinucleated giant cells and eosinophils, immune-complex deposition in dermal vessels.



Erythema nodosum

Q: In erythema nodosum, what history should be taken? What else do you like to examine?

A: As follows:

1. History of:
 - Drugs (see below).
 - Fever
 - Sore throat or tonsillitis (streptococcal tonsillitis).
 - Other infection (TB, leprosy and histoplasmosis).
 - Arthritis or arthralgia or other features of sarcoidosis.
 - GIT symptoms like diarrhoea, dysentery, pain abdomen, etc. (inflammatory bowel disease).
2. On examination:
 - Throat (tonsillitis).
 - LN (sarcoidosis, TB, lymphoma and fungal infection).
 - Liver, spleen (sarcoidosis and lymphoma).
 - Skin changes (lupus pernio in sarcoidosis, anaesthetic patch or erythematous or nodular lesion in leprosy).
 - Ulceration in mouth, genitalia (Behçet syndrome).
 - Evidences of rheumatic fever.

Q: What are the causes of erythema nodosum?

A: As follows:

- Sarcoidosis (usually in acute).
- Streptococcal beta-haemolyticus infection (throat).
- Primary pulmonary TB.
- Drugs (sulphonamide, penicillin, oestrogen-containing oral contraceptive pill, salicylates, barbiturates, sulphonylureas, bromides and iodides).
- Inflammatory bowel disease (Crohn disease, ulcerative colitis).
- Fungal infections (histoplasmosis and coccidioidomycosis, and is common in the USA).
- Protozoal (toxoplasmosis).
- Leprosy [erythema nodosum leprosum (ENL)].
- Idiopathic (up to 50% cases).
- Others: Brucellosis, rickettsial and mycoplasma infection, viral infection, pregnancy, lymphoma, cat-scratch disease, Behçet syndrome and SLE.

Q: What investigations are done in erythema nodosum?

A: As follows:

- CBC, ESR, PBF (leucocytosis in streptococcal infection, high ESR in TB).
- Antistreptolysin O (ASO) titre, throat swab for C/S, blood for C/S (in streptococcal infection).
- Chest X-ray (TB and sarcoidosis).
- MT and sputum for AFB (in case of TB).
- LN biopsy (sarcoidosis, lymphoma and TB).
- Inflammatory bowel disease [barium enema (double-contrast), sigmoidoscopy or colonoscopy, barium follow through].
- Other investigations: According to suspicion of cause.

Q: How to treat erythema nodosum?

A: As follows:

1. Treatment of primary cause (e.g. penicillin, if streptococcal infection). It is self-limiting, may resolve in 3–6 weeks.
2. Other treatment:
 - Rest.
 - Nonsteroidal anti-inflammatory drugs (NSAIDs) (indomethacin).
 - In severe cases, corticosteroid should be given.
 - Empirically, a short course of potassium iodide in a dose of 400–900 mg daily may be helpful.

Q: What is erythema induratum (Bazin disease)?

A: Erythema induratum of Bazin type is a nodular vasculitis (which is a multifactorial syndrome of lobular panniculitis), related to tuberculous origin. It is one of the sequelae of immunologic reactions against antigenic components of *Mycobacterium tuberculosis*, which spreads through blood. It represents a delayed-type hypersensitivity reaction to tubercle bacillus. Recently, hepatitis C virus has been suspected as a cause.

It is more common in women, aged 20–30 years, mostly occurring in lower extremities, usually in calves, may also be in shins. Differential diagnoses are chilblain, erythema nodosum, erythema nodosum leprosum, pancreatic panniculitis, lupus panniculitis, etc. Diagnosis is based on routine blood count, ESR, PCR and biopsy of the involved tissue.

Treated with antituberculous therapy. Steroid may be indicated. Potassium iodide is sometimes needed for local application. Complication of untreated or inadequately treated erythema induratum involves persistent ulceration. If treated properly, the prognosis is good.

Q: What are the differences between erythema nodosum and erythema induratum?

A: As follows:

	Points	Erythema nodosum	Erythema induratum
1.	Duration	Short	Long
2.	Site	Shin	Calf
3.	Occurrence	Lesions occur simultaneously	Lesions occur serially in crops

4.	Ulceration	Absent	Present
5.	Pain	More	Less
6.	Scarring	Absent	Present
7.	Cause	Multiple causes	Usually TB
8.	Histology	Septal panniculitis	Lobular panniculitis

N.B. Erythema nodosum is not vasculitic in origin; rather it is a septal panniculitis, where the inflammation is mostly in the septa of fat, with little or no vasculitis.



Erythema induratum

Leprosy

Presentation of a Case: 1

- Multiple nodules of variable size and shape involving right or left or both ear lobule, also face and nose. Skin is thick.

Differential diagnoses are:

- Post-kala-azar dermal leishmaniasis (PKDL).
- Lepromatous leprosy.
- Sarcoidosis.
- Drug rash.
- Acne rosacea.
- Dermatomyositis.

Presentation of a Case: 2

- Multiple hypopigmented patches of variable size and shape in the trunk, upper abdomen and back. No loss of sensation.

Differential diagnoses are:

- Fungal infection.
- Tinea versicolor.
- PKDL (early stage).
- Drug reaction.
- SLE.
- Lepromatous leprosy.
- Psoriasis.

Q: What **else** do you like to see?

A: Sensation in patch (loss in leprosy). Also, see nerve thickening (radial in humerus, ulnar in elbow, median in wrist, common peroneal in back of knee, posterior tibial and sural at ankle, and great auricular in posterior triangle in neck).

Q: What **investigations** are done to diagnose leprosy?

A: Slit skin smear for AFB staining, also skin biopsy. In tuberculoid type, epithelioid granuloma may be found. In lepromatous leprosy, *Mycobacterium leprae* may be found in skin macrophage (also Schwann cells and perineurium).

Q: What are the types of **classification** of leprosy?

A: There are five types:

- Tuberculoid leprosy (TT).
- Borderline tuberculoid (BT).
- Borderline leprosy (BB).
- Borderline lepromatous leprosy (BL).
- Lepromatous leprosy (LL).

Also, classified into two types:

- Paucibacillary: Skin smear for *Mycobacterium leprae* bacilli is negative or few TT and BT.
- Multibacillary: Skin smear for *Mycobacterium leprae* bacilli is positive BT, all BB, BL and LL.



Leprosy



Leprosy (hypopigmented patch and nodule in front)



PKDL



Leprosy (hypopigmented patch and nodule on the back)



Leprosy (nodule in dorsum and toe)



Erythema nodosum leprosum

Q: How to treat leprosy?

A: As follows:

- Paucibacillary (three to five skin lesions, skin smear negative or few, tuberculoid and BT): Rifampicin 600 mg monthly (supervised) **plus** dapsone 100 mg daily (self-administered) for 6 months.
- Multibacillary (more than five skin lesions, skin smear positive, BT, all BB, BL and LL): Rifampicin 600 mg and clofazimine 300 mg monthly (supervised) **plus** dapsone 100 mg and clofazimine 50 mg daily (self-administered) for 12 months.
- Paucibacillary single lesion: Ofloxacin 400 mg **plus** rifampicin 600 mg **plus** minocycline 100 mg, in single dose.

Q: What is erythema nodosum leprosum (ENL)? How it is treated?

A: It is a type 2 lepra reaction, which is due to immune complex deposition (**type 3** hypersensitivity reaction), occurs in BL and LL patient who produce antibodies and have a high antigen load. Characterised by fever, arthralgia and crops of small pink painful nodules on the face and limbs. Iritis and episcleritis are common. Other signs are neuritis, orchitis, myositis, bone pain, lymphadenitis and arthritis.

ENL may be the first manifestation of leprosy, 50% in lepromatous and 25% in BL, either during the course of the disease or more commonly in the second year of treatment. ENL may continue intermittently for several years.

Treatment:

- Antileprosy therapy must be continued.
- In mild cases, analgesics (aspirin 600 mg, 6 hourly).
- In severe cases, thalidomide (100 mg, 6 hourly). When symptoms improve, reduce the dose slowly over weeks or months, maintenance dose is 50–100 mg daily. It is a potent teratogenic

drug (avoid during pregnancy). If thalidomide is not available, prednisolone (20–40 mg) should be given, and reduce the dose over 1–6 months. Chloroquine can also be used. Increase the dose of clofazimine (300 mg daily) for few weeks. It will reduce the reaction and help to reduce the dose of prednisolone.

Q: What is lepra reaction?

A: It is defined as episodes of inflammation in the pre-existing lesion of leprosy. It may be the first manifestation of the disease. Lepra reaction may be insidious or rapid, destroying the affected tissue within hours. It is of two types: Type 1 and type 2 (see above).

Type 1 occurs in 30% borderline patients (BT, BB and BL) due to delayed hypersensitivity reactions. It occurs spontaneously or precipitated by treatment. Nerve function is lost rapidly, foot drop may occur overnight. Skin lesions become erythematous and peripheral nerves are painful. Reversal of reactions may occur spontaneously after starting treatment and also after completion of multidrug therapy.

Treatment:

- In mild case, aspirin 600 mg, 6 hourly.
- In severe case, prednisolone 40–60 mg daily; reduce the dose to 5 mg/day each month.

Superior Vena Caval Obstruction

The usual instructions are:

- Look at the patient. What are your findings? What else do you want to examine?

(Patient may be dyspnoeic or may have stridor.)

See the following points:

1. Face (oedematous or puffy, red, plethoric, suffused and cyanosed).
2. Eyes:
 - Periorbital oedema.
 - Red eyes, congested conjunctiva (bloodshot eyes).
 - Chemosis (conjunctival oedema).
3. Neck: Swollen and neck veins are engorged and nonpulsatile (in CCF, engorged and pulsatile).
4. Visible tortuous and dilated veins in chest wall and abdomen (see the flow is downwards).
5. Upper limb may be oedematous with prominent engorged veins.
6. Then examine the following points to find out the causes of superior vena cava (SVC) obstruction:
 - LNs for supraclavicular or cervical lymphoma or metastasis.
 - Thyroid may be enlarged (look for retrosternal thyroid, trachea shifted).
 - Clubbing (bronchial carcinoma).
 - Radiation mark in chest (bronchial carcinoma).
 - Chest (to see bronchial carcinoma).
 - Signs of Horner syndrome.
 - Ophthalmoscopy (dilated vessels, haemorrhage, exudate, rarely papilloedema).



SVC obstruction (engorged veins in chest)



SVC obstruction (engorged veins in arm)



SVC obstruction (engorged veins in abdomen)

Presentation of a Case:

- The face is puffy, plethoric and cyanosed.
- There is periorbital oedema; eyes are congested with chemosis.
- The neck veins are engorged and nonpulsatile.
- There are also engorged veins in chest wall and abdomen, and the flow is downwards.
- Both the arms are oedematous, clubbing with nicotine staining.
- Undersurface of tongue shows multiple venous angiomata.

Diagnosis is **SVC obstruction.**

Q: What **relevant** do you like to examine in this patient?

A: As follows:

- Chest (bronchial carcinoma).
- LNs (lymphoma and metastasis).
- Liver and spleen (lymphoma).
- Clubbing, nicotine stain (bronchial carcinoma).
- Thyroid (to see retrosternal thyroid).

Q: What are the **causes** of SVC obstruction?

A: Describe the causes considering the age:

- In the elderly or middle-aged, the causes are bronchial carcinoma and lymphoma.
- In young or early age, the cause is lymphoma.

Q: What are the **presentations** of SVC obstruction?

A: The patient may complain of:

- Breathlessness, cough, hoarseness of voice and dysphagia.
- Flushing, red, puffy and oedematous face.
- Headache (early morning), which becomes severe with coughing. May be syncope, dizziness or blackout, stupor, seizure (due to increased intracranial pressure).
- Symptoms are aggravated on lying down or bending forward (indicates mediastinal involvement).
- The patient may have stridor (tracheal compression), hoarseness of voice (recurrent laryngeal nerve involvement), Horner syndrome (cervical sympathetic chain involvement).

Q: What are the **causes** of death in SVC obstruction?

A: Death is due to:

- Respiratory obstruction.
- Intracranial haemorrhage.

Q: Tell **one investigation** that will help the diagnosis of SVC obstruction.

A: Chest X-ray (bronchial carcinoma and lymphoma).

Q: What **investigations** would you like to do?

A: As follows:

- Chest X-ray.
- Sputum for malignant cells.
- CT or MRI of chest, contrast venography or magnetic resonance venography (MRV).
- If LN, FNAC or biopsy.
- Others (according to suspicion of causes): Bronchoscopy and mediastinoscopy, and occasionally thoracotomy may be needed.

Q: How will you **treat** the case?

A: Treatment is according to cause:

- The commonest cause is bronchial carcinoma: Radiotherapy in non-small cell carcinoma and chemotherapy for small cell carcinoma.
- If lymphoma, treat accordingly (usually chemotherapy).
- To relieve oedema, intravenous frusemide, head should be raised. Dexamethasone may be used.
- To relieve severe obstruction, balloon angioplasty and expandable metallic stent may be used (placed in SVC) as palliative measure.

Causes of SVC obstruction

1. Bronchial carcinoma (the commonest, in 75%).
2. Lymphoma (early age, also in the elderly).
3. Other causes:
 - Any tumour in mediastinum, such as thymoma, germ cell tumour, metastasis to mediastinum.
 - Retrosternal thyroid.
 - Chronic fibrotic mediastinitis (which may be idiopathic or secondary to tuberculosis, histoplasmosis, pyogenic infection, radiation, drugs like methysergide used in migraine).

- Giant aneurysm of the aortic arch.
- Carcinoma of oesophagus.
- Rarely thrombosis, invasion by malignancy and chronic constrictive pericarditis.

N.B. Remember the following points:
- SVC obstruction of recent onset is likely to be due to malignancy.
- SVC obstruction of long-standing is due to nonmalignant origin.

Hirsutism

The usual instructions are:

- Look at the patient. What is your diagnosis? What else do you want to see?

Presentation of a Case (a Female Patient)

- There is hirsutism.
- Patient is obese with Cushingoid face (if any).



Hirsutism in Cushing syndrome

Q: What are the **causes** in this case?

A: Describe according to your finding considering the age:

1. If Cushingoid face, diagnosis is Cushing syndrome.
2. If patient is obese and young, diagnosis is polycystic ovarian syndrome (PCOS).
3. Other causes:
 - Idiopathic (in most cases).
 - Familial, racial and postmenopausal.
 - Drugs (see below).
 - Late-onset congenital adrenal hyperplasia.
 - Adrenal causes (carcinoma or androgen-secreting adrenal tumour).
 - Ovarian cause (androgen-secreting ovarian tumour).

Q: What **other history** would you like to take?

A: As follows:
- Family history.
- If Cushing syndrome is suspected: History of prolonged intake of steroid.
- Age of onset of hirsutism: In younger and early age, common cause is PCOS. So history of amenorrhoea, weight gain, infertility, etc. should be taken. In elderly or postmenopausal.
- Weight gain.
- Drug history: Steroids, androgen, phenytoin, cyclosporine, minoxidil.
- Rate of progression of hirsutism.
- Thinning of scalp hair.

Q: What **else** do you want to see in this case of hirsutism?

A: As follows:
1. Hair in other parts of the body, chest and back (increased); hair in midline below the umbilicus to groin (increased); excess hair in the upper and lower limbs.
2. Evidence of **virilisation**:
 - Male baldness (frontal baldness).
 - Male body habitus.
 - Deepening of voice.
 - Others (clitoromegaly, atrophy of breast, male pattern of pubic hair, acne, greasy skin).
3. Abdominal mass (PCOS, ovarian tumour, adrenal carcinoma).
4. History of drugs causing hirsutism (see below).
5. Menstrual history (amenorrhoea in PCOS).

Q: What is the **difference** between hirsutism and hypertrichosis?

A: As follows:
- Hirsutism is male pattern of hair growth in women due to excess of androgen.
- Hypertrichosis is generalised excess hair growth in any sex, which is nonandrogenic in origin.

Q: What is **hirsutism**? What are the **causes**?

A: Hirsutism is excess growth of terminal hair in women as male pattern due to excessive secretion of androgen.

Hair growth in beard or chin or moustache. Also in breast, chest, axilla, abdominal midline, pubic and thigh area; all are related to androgen. Increase in hair growth indicates excessive androgen, either adrenal or ovarian in origin.

Causes of hirsutism:

- Hirsutism without virilisation.
- Hirsutism with virilisation.

Hirsutism without virilisation:

- Idiopathic (in most cases).
- Familial.
- Drugs (steroid, phenytoin, cyclosporine, androgen, minoxidil and progesterone).
- Others: PCOS (in mild cases, hirsutism is more and virilisation is less), acromegaly and porphyria cutanea tarda.

Hirsutism with virilisation:

- Ovarian causes: PCOS (severe case), androgen-secreting ovarian tumour, arrhenoblastoma.
- Adrenal causes: Late onset of congenital adrenal hyperplasia, Cushing syndrome, adrenal carcinoma or androgen-secreting adrenal tumour.

Q: How will you **investigate** a case of hirsutism?

A: As follows:

- Good history (see above).
- History of drugs (see above).
- Family history.

After exclusion of these, causes may be ovarian or adrenal:

- Blood for testosterone, LH, FSH and prolactin. If testosterone is high (twice the normal) associated with low LH and FSH, it is unlikely to be PCOS and idiopathic hirsutism.

Next, USG of abdomen to see ovarian or adrenal mass.

A. In case of **ovarian origin,** perform the following test:
 - If LH is high and FSH is normal or high (ratio of LH:FSH is 2 or 3), suggest PCOS.
 - Sex hormone binding globulin (SHBG) (high).
 - Androgens (high, but testosterone is normal or low).
 - Other tests such as CT scan, MRI and laparoscopy may be done.

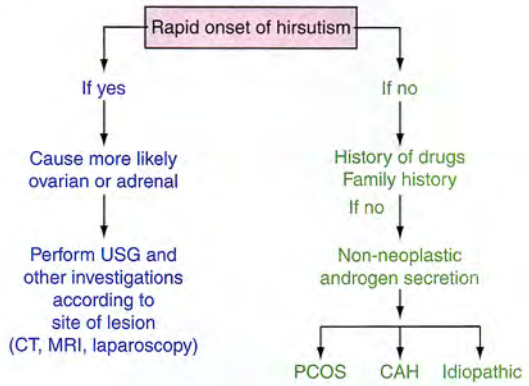
B. In case of **adrenal origin,** do the following tests:
 - If adrenal carcinoma or adenoma, urinary 17-ketosteroid is high.
 - Dexamethasone suppression test may be done (for failure of suppression).



Hypertrichosis

- In congenital adrenal hyperplasia, serum 17-hydroxyprogesterone is high, and also there is high pregnanetriol and ACTH.
- Other tests such as CT scan, MRI and laparoscopy may be done.

Another method of investigation



N.B. A good history regarding hirsutism is essential:
- If the onset is shortly after menarche, tumour is unlikely.
- If it occurs in childhood, more chance of underlying disease.
- If menstruation is regular, more likely to be constitutional rather than tumour or other pathology.
- Greater the menstrual abnormality (irregular or cessation), more likely there is a serious disease (ovarian or adrenal).
- Rapid onset, prepubertal or late onset is suggestive of underlying disease (ovarian or adrenal).
- Increased libido and signs of virilisation indicates increased androgen.

Q: How to **treat** hirsutism?

A: As follows:

1. Treatment of primary cause. If due to drug, it should be stopped.

2. Local therapy:
 - Plucking, bleaching, depilatory cream, shaving, electrolysis, epilation.
 - Topical eflornithine cream applied locally for 6 months is also effective.
3. Systemic therapy (use in severe cases):
 - Cyproteroneacetate(antiandrogen)50–100mg daily for 1–14 days of each cycle. In women of childbearing age, contraception is essential.
 - Oestrogen (in oral contraceptive) is helpful in idiopathic or PCOS. It reduces free androgens by increasing SHBG, where this is low.
 - Other antiandrogens: Spironolactone, flutamide or finasteride are also helpful.



Hirsutism (front view)



Hirsutism (side view)



Hirsutism in PCOS

Polycystic Ovarian Syndrome

Usual instructions:

- Perform the general examination, or,
- Look at the patient. What are your findings? (Usually hirsutism, obesity in a young girl)

Presentation of a Case (a Female Patient)

- This young patient is obese and there is hirsutism.

My diagnosis is: In this young lady with obesity and hirsutism, more likely it is a case of PCOS.

Q: What are the **differential diagnoses?**

A: As follows:

1. PCOS.
2. Congenital adrenal hyperplasia (late onset. In such case, there is raised serum 17α-hydroxyprogesterone).
3. Cushing syndrome (other features are present).
4. Virilizing tumour of the adrenal or ovary (rapid onset of signs of virilization, very high serum testosterone).
5. Obesity.
6. Hypothyroidism.
7. Drugs (e.g. danazol, androgenic progestins).

Q: What is polycystic ovarian syndrome (PCOS)?

A: It is syndrome in which there are multiple cysts in the ovary and hyperandrogenemia, characterized by:

- Amenorrhoea or oligomenorrhoea.
- Obesity.
- Hirsutism.
- Infertility (due to anovulation).
- Virilisation (in severe cases).

PCOS (originally called severe form of Stein–Leventhal syndrome) is associated with increased LH due to abnormality of pulsatile **GnRH** secretion (there is chronic anovulation without specific underlying disease of adrenal, pituitary or ovary).

Q: What are the **diagnostic criteria** of PCOS?

A: Two of the following three features are required for PCOS to be diagnosed:

- Menstrual irregularities (oligomenorrhoea or amenorrhoea).
- Clinical or biochemical evidence of androgen excess.
- Multiple cysts in the ovaries (most readily detected by transvaginal ultrasonography).

Q: What **investigations** should be done to diagnose PCOS?

A: As follows:

1. USG as first investigation (it shows thickened capsule, multiple 3–5 mm cyst and hyperechogenic stroma).
2. Biochemical tests:
 - Serum testosterone (usually high).
 - LH (increased).
 - FSH (normal or low, in a ratio of LH:FSH > 2 or 3).
 - Androgens (androstenedione and dehydroepiandrosterone are increased).
 - SHBG: Decreased.
 - Prolactin (slightly increased, rarely greater than 1500 mU/L).
 - Oestrogen (oestradiol is usually normal).
3. To exclude other cause, investigations should be done according to suspicion:
 - Serum 17 α OH progesterone [high in late-onset congenital adrenal hyperplasia (CAH)].
 - CT or MRI of adrenal (in suspected tumour).
 - Dexamethasone suppression test.
 - A short ACTH stimulation test with measurement of 17α-hydroxyprogesterone is done to diagnose CAH.

Q: How to **treat** PCOS?

A: As follows:

1. General measures:
 - Reduction of weight.
 - Regular exercise and diet control.
2. For hirsutism, as described above.
3. For fertility:
 - Metformin: May improve ovulation and achieve conception.
 - Clomiphene 50–100 mg/day, from days 2–6 of cycle. Dexamethasone 0.5 mg at bedtime with clomiphene may increase the likelihood of ovulation by suppressing ACTH.
 - If no response to clomiphene, metformin may be added, 500 mg three times daily. It may enhance ovulation.
 - Prednisolone in reverse circadian rhythm (2.5 mg in the morning and 5 mg at bedtime) may suppress pituitary ACTH, upon which adrenal androgen partly depend. With this therapy, regular ovulatory cycle often ensue.
4. For menstrual disturbance:
 - Metformin 500 mg three times daily improves menstrual cycle and ovulation. Also may improve hirsutism and obesity.
 - Cyclical low-dose oestrogen or progesterone administration.
 - Patient who does not desire pregnancy should get medroxyprogesterone 10 mg daily orally for first 10 days of each month. It ensures regular shedding of endometrium.
5. Wedge resection or laser surgery of ovary or laparoscopy ovarian drilling may be done in some cases.
6. For obesity: Metformin may be used.

N.B. Adrenal androgen is under control of ACTH and ovarian androgen is under control of LH.

Q: What are the **complications** in PCOS?

A: As follows:

- Hyperinsulinaemia and insulin resistance.
- Glucose intolerance.
- Type 2 DM.
- Hypertension, dyslipidemia and cardiovascular risk.

Leg Ulcer

Usual instructions are:

- Look at the leg; or, examine the leg; or, perform general examination.

Look at the following points carefully:

- Site of ulcer (one or both legs or feet or tip of toes).
- Single or multiple.
- Margin (irregular, raised, undermined, everted and punched out).
- Any slough or necrotic area or gangrene.
- Oozing (pus or serous fluid) or dry area.
- Any blister (rupture).
- Surrounding area (healthy or pigmented).
- Temperature (cold or warm).
- Pulse (absent or bounding).
- Sensation (light touch, pain, vibration and position sense).



Leg ulcer in SLE



Leg ulcer (enlarged)

Presentation of a Case

- There is ulcer (ulcers) involving one or both shin of legs or feet, with a clear margin; some parts are necrosed or gangrenous, with oozing.
- Leg is cold, pulse is absent, sensation is normal.
- Joint abnormality, trophic ulcers and gangrene (mention, if any).

Q: What do you think about the causes of leg ulcer?

A: Mention the causes according to the age of the patient:

If the patient is middle-aged or elderly, the causes are:

- Trauma.
- Atherosclerosis (in old age).
- DM.
- Peripheral neuropathy.
- Infection (TB, pyogenic infection, leprosy, leishmaniasis).
- Pyoderma gangrenosum.

If the patient is of younger or of early age, the causes are:

- As above (except atherosclerosis).
- Collagen disease (SLE, RA, Felty syndrome).
- Haematological diseases include sickle cell anaemia, thalassaemia, hereditary spherocytosis.

Q: What **history** do you like to take in leg ulcer?

A: History of trauma, smoking, DM, hypertension, evidence of infection, collagen diseases.

Q: What **investigations** should be done in leg ulcer?

A: As follows:

- Hb%, total count (TC), differential count (DC) and ESR.
- Blood sugar.
- Lipid profile (in atherosclerosis).
- Pus (if any), for C/S, AFB, Leishman–Donovani (LD) bodies.
- Doppler USG of lower limb vessels.
- Biopsy.
- X-ray of leg (calcification in artery may be seen).
- Arteriography.
- Others: According to suspicion of causes, e.g. anti-nuclear antibody (ANA), cold agglutinin and rheumatoid arthritis (RA) test.

Q: How to **treat** leg ulcer?

A: As follows:

- Smoking should be stopped.
- Control of DM, hypertension, obesity (if any).
- Treatment of primary cause.
- Local care (cleaning, removal of necrotic tissue and dressings).
- Antibiotic, if any infection.
- Consult with chiropodist.
- Low-dose aspirin.
- In some cases, surgery (balloon dilatation) and if necessary, amputation.
- Education to the patient: Avoid walking bare foot, avoid tight shoes, use appropriate footwear, crutch may be used to avoid weight bearing, cutting toe nails carefully, look for blisters in foot, which should be cleared.

Causes of leg ulcer

- Traumatic.
- Infection (pyogenic, TB, leprosy and leishmaniasis).
- Arterial (ischaemic, occurs more on lateral side called Buerger disease) causes are atherosclerosis, peripheral vascular disease and arterial occlusion, and arterial ulcer is usually tender, punched-out ulcer on leg, cold skin, loss of hair, and absent or reduced pulse.
- Venous ulcer occurs usually due to varicose vein. (Venous ulcer is usually around malleoli or in medial side; the leg is oedematous. There may be wet gangrene, pigmentation and eczema.)
- Neuropathic ulcer (DM, tabes dorsalis, syringomyelia, leprosy, polyneuropathy due to any cause).
- Collagen disease (SLE, RA, Felty syndrome, cryoglobulinaemia, polyarteritis nodosa).
- Haematological (sickle cell anaemia, thalassaemia, hereditary spherocytosis, paroxysmal nocturnal haemoglobinuria, thrombotic thrombocytopaenic purpura and macroglobulinaemia).
- Neoplastic (squamous cell carcinoma, basal cell carcinoma, lymphoma and Kaposi sarcoma).
- Pyoderma gangrenosum.



Varicose ulcer



Ulcer in foot

Pyoderma Gangrenosum

Instruction to the examinee:

- Look at the foot or leg; or, perform general examination.



Pyoderma gangrenosum (early stage)

Presentation of a Case

- There is a large necrotic ulcer with ragged bluish-red, gangrenous overhanging margin, purulent surface with pustules and plaque.



Pyoderma gangrenosum (skin peeled off, severe advanced stage)

Diagnosis is **pyoderma gangrenosum.**

Q: What are the differential diagnoses?

A: As follows:

- Trauma.
- Venous ulcer.
- Infection (TB, pyogenic infection, leprosy, leishmaniasis).
- Collagen disease (SLE, RA, Felty syndrome, cryoglobulinaemia).

- Vasculitis (polyarteritis nodosa, Behcet syndrome, Wegener granulomatosis).
- Haematological (sickle cell anaemia).
- Neoplastic (squamous cell carcinoma, basal cell carcinoma, cutaneous lymphoma).

Q: Ask one **question** or what **history** do you like to take?

A: History of diarrhoea or bloody diarrhoea (suggestive of inflammatory bowel disease).

Q: What is **pyoderma gangrenosum**? What are the **causes**?

A: It is a noninfective, necrotising ulceration with clear-cut bluish-red overhanging edge, usually in the shin. The lesion starts as a blister or pustule, breaks down centrally, expands rapidly to an ulcer with indurated or undermined purplish or pustular edge.

It occurs commonly in legs, but may be anywhere in the body surface, may be single or multiple. It is common in adults (25–54 years). Diagnosis is usually clinical, and biopsy shows nonspecific findings.

Q: What is the **pathogenesis** of pyoderma gangrenosum?

A: Actual pathogenesis is unclear; there is depression of immune system. Failure of macrophage to respond to tissue injury or to clear the obnoxious agent is another factor.

Q: What are the **types** of pyoderma gangrenosum?

A: There are four types:

- Ulcerative.
- Pustular.
- Bullous.
- Vegetative.

Q: What **investigations** will you do?

A: As follows:

1. CBC, ESR.
2. Blood sugar.
3. Biopsy from the lesion.
4. Other investigations according to suspicion of cause:
 - For IBD: Barium enema, colonoscopy.
 - For collagen disease: ANA, anti-dsDNA, antiphospholipid antibody.
 - For vasculitis: Perinuclear antineutrophil cytoplasmic antibodies (pANCA), cytoplasmic antineutrophil cytoplasmic antibodies (cANCA).
 - For myeloma: Protein electrophoresis, bone marrow, etc.

Q: What is the **treatment** of pyoderma gangrenosum?

A: As follows:

1. Treatment of underlying diseases.
2. General measures:
 - Control of infection.
 - Local dressing
 - Analgesic for relief of pain.
3. Topical:
 - Highly potent corticosteroid may be sufficient in some patients. Triamcinolone may be injected into the ulcer edge (alone or with systemic treatment).
 - Tacrolimus may be given.
4. Systemic:
 - Oral prednisolone in high dose is needed in most patients. In some patients, methylprednisolone 1 gm intravenous (IV) for 3 days may be given initially for quick remission.
 - Minocycline 100 mg/day may help to reduce the dose of steroid.
 - Immunosuppressive agents like ciclosporin, tacrolimus or azathioprine may be used to reduce steroid dependence or in resistant cases.
 - Anti-TNF α (infliximab, etanercept) may be used if others fail.
 - Dapsone may be used in milder cases.
 - Other drug therapy: Colchicine, clofazimine, cyclophosphamide, mycophenolate mofetil, etc. These may help in few patients.

Causes of pyoderma gangrenosum

- Inflammatory bowel disease: Ulcerative colitis (common), less in Crohn disease.
- RA.
- Polycythaemia rubra vera.
- Chronic granulocytic leukaemia (also in acute granulocytic leukaemia).
- Multiple myeloma and other paraproteinaemias (especially, IgA type).
- Myelofibrosis.
- Wegener granulomatosis.
- Chronic active hepatitis.
- HIV infection.
- Idiopathic in >20% cases.

N.B. In ulcerative colitis, pyoderma gangrenosum indicates severe disease. It may precede the onset of inflammatory bowel disease. Healing parallels with cure of ulcerative colitis and colectomy allows rapid healing.

Diabetic Foot

Usual instruction:

- Look at the foot of this diabetic patient. Or, do the general examination of this diabetic patient.

Look carefully the following points:

Inspection:

- Ulcer (site, single, multiple, oozing, gangrene and the surrounding area).
- Look at the tip of all toes, sole and spaces between the toes.
- If gangrene is present, see whether it is dry or wet, and the demarcation between healthy and unhealthy skin.
- Colour change of skin and hair loss.
- Amputation of toe (may be).
- Pigmented scar, small round plaques with raised border lying in a linear fashion over shin (diabetic dermopathy).
- Necrobiosis lipoidica diabeticorum (central yellow with raised margin, telangiectasia at the margin).
- Joints (Charcot joint or joint swelling).
- Thigh wasting, atrophy or hypertrophy (insulin therapy).

Palpation: Ask the patient whether the foot is sore.

- Temperature (warm or cold, and compare with other foot).
- Pulse (arteria dorsalis pedis and posterior tibial), if reduced, absent or bounding.
- Sensation, if reduced or absent (see light, touch, pain, joint sense).
- Reflex, if reduced or absent, see also plantar response.
- Vibration and position sense (may be lost due to the posterior column lesion called diabetic pseudotabes).
- In some cases, test for proximal myopathy (there may be diabetic amyotrophy, which shows asymmetrical wasting of thigh).



Diabetic ulcer in dorsum (with infarction and cellulitis)



Diabetic ulcer in sole (without gangrene)



Diabetic ulcer in dorsum (with gangrene and oozing)



Diabetic ulcer in sole (with gangrene)

Presentation of a Case

- There is an ulcer (ulcers) involving dorsum of right or left foot, toes (if any) (Mention if there is any gangrene and point out whether it is dry or wet).
- There is also pigmented area surrounding the ulcer extending up to... (mention the area) with loss of hair and shine.
- Foot is cold.
- Pulse is absent.
- Loss of sensation in foot, leg up to... (mention the area).

With this finding, my **differential diagnoses** are:

- Traumatic.
- DM (diabetic foot).
- Atherosclerosis.
- Infective (TB, leprosy and leishmaniasis).
- Buerger disease.
- Vasculitis [collagen disease: SLE, polyarteritis nodosa (PAN) and RA].

Q: What are the **causes** of ulcer in DM?

A: As follows:

- Ischaemia.
- Neuropathy.
- Combined ischaemia and neuropathy.
- Secondary infection.

Q: What is the **pathology** of ischaemic ulcer?

A: As follows:

- Usually microangiopathy.
- Associated atherosclerosis of large and medium vessels.

N.B. If the ulcer is painful, the cause is vasculitis and if it is painless, the cause is neuropathic.

Q: What are the findings, if the ulcer is due to **neuropathy**?

A: As follows:

- Ulcer is painless and mostly plantar.
- Area is warm, dry and pink.
- Pulse: Present and may be bounding.
- Sensory function: Reduced or absent. Vibration sense: Reduced or absent.
- Reflexes: Reduced or absent, plantar: Absent or equivocal.

Q: What are the findings, if the ulcer is due to **ischaemia**?

A: As follows:

- Ulcer is painful, over heels and toes.
- Area is cold, shiny, atrophied and loss of hair.
- Pulse: Absent or reduced.
- Sensory function: Normal.
- Reflexes: Normal.

Q: What are the **findings**, if the ulcer is due to **combined** neuropathy and ischaemia?

A: In such case, the findings are:

- Ulcer is on foot and callosities and pressure points.
- Loss of arch of foot.
- Sensory loss of all modalities in stocking pattern.
- Loss of pulsation.
- Foot is cold, shiny; and there is loss of hair.

Q: How to **prevent** diabetic foot ulcer?

A: Along with good control of diabetes, ensure the following:

1. Advice to all diabetic patients:
 - Inspect and wash feet every day.
 - Cut toe nails regularly, very carefully.
 - If skin is dry, use moisturizer.
 - Wear suitable good-fitting shoes.
 - Check footwear for foreign bodies.
 - Change socks or stockings every day.
 - Avoid walking barefoot.
 - Cover minor cuts with sterile dressings.
 - Do not burst blisters.
 - Avoid over-the-counter corn or callus remedies.
2. Additional advice to high-risk patients:
 - Do not attempt corn removal.
 - Avoid high and low temperatures.
3. Involve a podiatrist in the care of the patient.
4. Special footwear should be used in Charcot neuroarthropathy.

Q: How to **treat** a case of diabetic ulcer?

A: As follows:

- Good control of DM.
- Smoking should be stopped.
- Local dressing and removal of dead tissue.
- Antibiotic to control secondary infection.
- Consult with chiropodist.
- Surgery may be required (removal of callus, amputation or angioplasty).
- Patient education: Avoid barefoot, tight shoes, careful cutting of nails, avoid weight bearing.
- Other measures: As in foot ulcer.
- Liaison should be maintained among physician, chiropodist and surgeon.

Q: What are the **features** of diabetic foot?

A: As follows:

1. Neuropathic: Ulcer, sepsis, abscess, osteomyelitis, digital gangrene, Charcot joint.
2. Ischaemic: Ulcer, sepsis, gangrene.

Q: What are the **differences** between ischaemic ulcer and neuropathic ulcer?

A: As follows:

Features	Neuropathic ulcer	Ischaemic ulcer (arterial)
Symptoms	No pain. Paraesthesia or tingling may be present.	Pain, history of claudication.
Foot	High arched, clawing of toes, no trophic change	Dependant rubor, trophic changes are present (atrophy and loss of hair)
Area	Warm, dry and pink	Cold, shiny
Pulse	Bounding	Absent or reduced
Sensation	Reduced or absent	Normal
Ulcer	Painless and mostly plantar	Painful, over heels and toes
Reflex	Reduced or absent, equivocal plantar response	Normal

N.B. Doppler ultrasound study of the lower limb vessels and femoral angiography may be needed to see the localized area of occlusion. Either bypass surgery or angioplasty may be needed.

Causes of Neuropathic Ulcer

- Leprosy.
- DM.
- Polyneuropathy (due to any cause).
- Tabes dorsalis.
- Syringomyelia.
- Amyloidosis.
- Porphyria.
- Progressive sensory neuropathy.

Diabetic Amyotrophy

The usual instructions are:

- Look at the thigh. What are your findings?

Presentation of a Case

- There is wasting in right or left thigh (patient is cachexic or emaciated).

Q: What is the likely underlying **disease**?
A: Diabetes mellitus.

Q: What is **diabetic amyotrophy**?
A: A type of motor neuropathy in diabetic patient, characterised by asymmetrical wasting of muscles, usually involving the quadriceps (also in upper limb). Affected area may be tender, commonly accompanied by severe pain in anterior aspect of thigh.

It may be the first presentation of DM. The patient is occasionally cachexic (neuropathic cachexia) and extremely ill, unable to get out of bed. Hyperaesthesia or paraesthesia is common. There is reduction of muscle power, tone, loss of knee jerk with occasional extensor plantar response on the affected side. Cerebrospinal fluid (CSF) protein is increased.



Diabetic amyotrophy

Q: Where is the **site of lesion** or **cause** of diabetic amyotrophy?
A: It is thought to involve acute infarction of lower motor neuron of lumbosacral plexus.

Q: In which **type** of diabetes is it common?
A: It is more common in type 2 DM. It is common in elderly.

Q: How to **treat** diabetic amyotrophy?
A: As follows:

- Good control of DM.
- Intensive insulin therapy.
- For pain amitriptyline, imipramine or carbamazepine. Aldose reductase inhibitor may help.

Q: What is the **prognosis?**

A: Prognosis is good, usually recovers, but may take a long time (over months to 2 years).

Q: What are the **causes of unilateral wasting of leg?**

A: As follows:

- Diabetic amyotrophy.
- Old poliomyelitis.
- Arthritis or trauma.
- Cerebral palsy.
- Disc prolapse.

Lipodystrophy of Thigh

The usual instructions are:

- Look at the thigh. What are your findings?

There may be two findings in the thigh, together called lipodystrophy:

- Lipoatrophy.
- Lipohypertrophy.

Presentation of a Case (Lipoatrophy or Lipohypertrophy of Thigh)

- There is atrophy or wasting or hypertrophy of muscle of thigh (right or left) with multiple needle puncture marks.

Diagnosis is **lipoatrophy** or **lipohypertrophy** (mention which one).



Diabetic lipohypertrophy



Diabetic lipoatrophy



Diabetic bullae



Diabetic dermopathy

Q: What is the **underlying diagnosis?**

A: The patient is diabetic, receiving insulin injection.

Q: What is **lipoatrophy?**

A: It is the localised atrophy of subcutaneous fat due to repeated injection of unpurified animal insulin caused by immunogenic component of insulin.

Treated by injection of pure human insulin at the margin and centre of the affected area, which results in restoration of normal contour. It is rare now due to less use of animal insulin.

Q: What is **lipohypertrophy?**

A: It is the localised hypertrophy of subcutaneous fat due to repeated injection of purified insulin at the same site. It is caused by continued lipid synthesis at the affected site, and is treated by changing the site of injection.

Q: What are the **skin changes** in DM?

A: As follows:

- Necrobiosis lipoidica diabeticorum.
- Diabetic dermopathy (atrophic pigmented patch in skin, precipitated by trauma associated with neuropathy).
- Ulcer or gangrene.
- Secondary infections (boil, carbuncle and candidiasis).
- Acanthosis nigricans.
- Xanthelasma.
- Granuloma annulare.
- Lipoatrophy and lipohypertrophy.
- Diabetic bullae.
- Others: Vitiligo, xanthoma and peripheral anhydrosis.

Causes of Lipoatrophy of Skin

- DM (receiving insulin injection).
- Localised scleroderma or morphea.
- Chronic relapsing panniculitis.
- Mesangiocapillary glomerulonephritis.
- HIV.

Necrobiosis Lipoidica Diabeticorum

The usual instructions are:

- Look at the leg. What are your findings?

Presentation of a Case

- There is sharply demarcated, atrophied skin or plaque in the skin of shin with shiny surface and waxy yellow centre, brownish-red margin with surrounding telangiectasia.

Diagnosis is **necrobiosis lipoidica diabeticorum.**

Q: What are the **differential diagnoses?**

A: As follows:

- Localised scleroderma.
- Sarcoidosis.
- Polyarteritis nodosa.
- Granuloma annulare.
- Pyoderma gangrenosum.

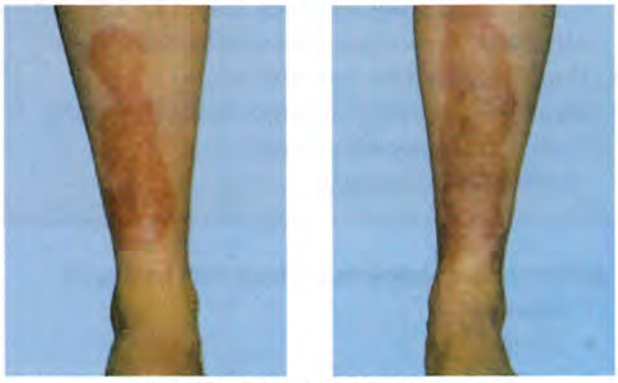
Q: What is **necrobiosis lipoidica diabeticorum?**

A: Plaque-like lesion with central yellowish area surrounded by brownish border on the anterior surface of leg. May be shiny, atrophic skin with telangiectasia. Fibrosis with scarring from previous ulceration may be seen.

This is a rare finding in DM (<1%), may be in pre-diabetic and in 50%, without diabetes. But 85% cases with necrobiosis lipoidica diabeticorum develop DM.

It is two to three times common in females, usually in young adult or early middle life. The cause is unknown, may be due to small vessel damage.

Histology shows necrosis of collagen, infiltration with epithelioid cells, giant cells with glycogen and lipid deposition.



Necrobiosis lipoidica diabeticorum

Treatment:

- Good control of DM.
- Dressing, local application or injection of steroid may be helpful.
- Psoralen + UVA (PUVA) may be helpful.
- Surgery with skin grafting.
- Low-dose aspirin, occasionally pentoxifylline may be helpful.

It may take long time to heal.

Unilateral or Bilateral Leg Swelling

Usual instructions:

- Look at the lower limbs. Or, examine the lower limbs.

Look carefully at the following points:

Inspection:

- Swelling, extent of swelling (right or left).

- Veins (engorged or varicose veins).
- Scratch mark.
- Pigmentation.
- Purpura.
- Hair change.
- Trophic ulcer.
- Look at the back of the leg.
- See associated joint swelling, clubbing and cyanosis.

Palpation:

- Temperature (warm or cold).
- Pulse (arteria dorsalis pedis, posterior tibial and popliteal artery).
- Oedema (pitting or nonpitting).
- Calf tenderness and localised swelling (DVT, ruptured Baker cyst).
- Homans sign (may be dangerous, with risk of pulmonary embolism).
- Associated LNs (popliteal, inguinal).

Presentation of a Case

- Right or left leg is swollen extending up to... (mention the site).
- Skin is rough, scaly and thick; loss of lusture and hair. There is excoriation or scratch mark.
- Nonpitting oedema (woody texture).
- Local temperature is normal or cold or warm. There is no lymphadenopathy.
- Arterial pulse is normal.

Diagnosis is **lymphoedema,** which may be due to:

- Filariasis.
- Trauma.
- Recurrent lymphangitis or cellulitis.
- Neoplasm.
- Surgery.
- Radiation.
- Primary lymphoedema.



Lymphoedema of left lower limb



Unilateral lymphoedema (left)



Bilateral leg swelling



Bilateral lymphoedema

Q: What are the differential diagnoses of unilateral leg swelling?

A: As follows:

- Lymphoedema.
- DVT.
- Angioneurotic oedema.

- Ruptured Baker cyst.
- Chronic venous insufficiency.
- Traumatic.
- Compartment syndrome following trauma or surgery (requires immediate fasciotomy).

N.B. Unilateral swelling in arm may occur following mastectomy or radiotherapy.

Q: What are the causes of **bilateral** leg swelling?

A: As follows:

- Oedema due to any cause (CCF, nephrotic syndrome, cirrhosis of the liver, hypoproteinaemia).
- Myxoedema.
- Some cases of lymphoedema.
- Acromegaly.
- Inferior vena caval (IVC) obstruction (dilated tortuous veins in the lower limbs with upwards flow).
- Iliac vein thrombosis.
- Pregnancy.
- Drugs (calcium channel blockers, such as nifedipine or amlodipine).

Q: How will you **investigate** a patient with bilateral pedal oedema?

A: As follows:

1. Routine:
 - Urine R/E.
 - Complete blood count.
 - Serum creatinine.
 - Serum total protein; A:G ratio.
2. Other according to suspicion:
 - If CCF: ECG, chest X-ray, echocardiogram.
 - If nephrotic syndrome: 24-h urinary protein, renal biopsy if needed.
 - If myxoedema: TSH, FT_3, FT_4.
 - Ultrasonogram of whole abdomen.
 - Duplex study of both lower limbs.

Q: How will you **investigate** a patient with unilateral pedal oedema?

A: As follows:

1. Routine:
 - Urine R/E.
 - CBC.
2. Other according to suspicion:
 - Colour Doppler ultrasonogram of the affected limb (may be helpful to see DVT or venous insufficiency).
 - For lymphoedema (see below).

Q: What are the causes of nonpitting oedema?

A: As follows:

- Lymphoedema due to any cause.
- Myxoedema.

Q: Why there is **nonpitting oedema**?

A: Normally, small amount of albumin filtered through the capillaries is absorbed through lymphatics. In lymphatic obstruction, water and solutes are reabsorbed into the capillaries, but the protein remains. Fibrosis occurs in the interstitial space and the area becomes hard or thick.

Q: What are the causes of **acute unilateral** leg swelling?

A: As follows:

- Deep venous thrombosis.
- Ruptured Baker cyst.
- Cellulitis.
- Trauma.
- Angio-oedema.

Causes of Lymphoedema

1. Primary:
 - Secondary to agenesis or hypoplasia.
 - Hereditary (Milroy disease).
 - Associated with Turner syndrome, Noonan syndrome and yellow nail syndrome.
2. Secondary:
 - Recurrent lymphangitis or cellulitis.
 - Filariasis.
 - Trauma.
 - Tuberculosis.
 - Neoplasm.
 - Surgery (in the arm, it may be due to mastectomy).
 - Radiation.
 - Burn.

Q: What **investigations** do you suggest in lymphoedema?

A: As follows:

- Hb%, TC, DC, ESR (eosinophil may be high in filariasis).
- Blood film to see filaria (usually at night, for *Wuchereria bancrofti* and *Brugia malayi*). Also, found in chylous fluid and hydrocoele fluid.
- Provocation test (by giving diethylcarbamazine, 50 mg orally; see the blood film for filaria after 30 minutes).
- Compliment fixation test (CFT) or indirect fluorescent antibody test (IFAT) for filaria.
- Filarial antigen detection.
- Lymphoscintigraphy.
- Lymphangiogram.
- Other investigations to exclude other disease: USG of whole abdomen, Doppler ultrasound

scans of lower limbs (to exclude deep venous thrombosis), CT scan or MRI of abdomen, chest X-ray and MT.

Q: How to treat lymphoedema?

A: No curative treatment. Mainly supportive to reduce the swelling and control discomfort.

1. Intermittent elevation of the extremity by placing pillows, mainly during sleeping.
2. Compression treatments:
 - Elastic sleeves or stockings.
 - Bandages: The extremity is wrapped tightly to remove lymph out of the limb.
 - Massaging the affected part either by hand or by pneumatic compression can be useful.
 - Exercises.
3. Surgical treatment: May be used to remove excess fluid and tissue in severe cases.
4. Secondary infections of skin and tissues associated with lymphoedema should be treated with antibiotics.
5. If filariasis is suspected, diethylcarbamazine is used.

Q: What is angio-oedema?

A: It is the swelling of dermis and subcutaneous tissue. There are two types: hereditary and acquired.

Q: What is hereditary angio-oedema?

A: It is a disorder inherited as autosomal dominant due to C1-esterase inhibitor deficiency. There is involvement of the blood vessels. Family history is present. Attack is usually recurrent; episodes of oedema in the skin of face, limbs and mucosa of the larynx can occur. Laryngeal oedema may be life threatening. Recurrent abdominal pain may occur. Nonhereditary form may occur in lymphoproliferative disorder.

Diagnosis:

- Serum C2 and C4 (both low).
- Measurement of C1 esterase inhibitor (low).

Treatment:

1. In acute attack:
 - Epinephrine should be used in life-threatening reactions.
 - C1 inhibitor concentrate should be given, if available. A newer medicine called ecallantide may be used instead.
 - Fresh frozen plasma containing C1 inhibitor may be used.
2. To prevent recurrent attack, danazol or stanozolol may be given. It stimulates the liver, which synthesises the enzyme. (This drug may cause fluid retention, menstrual irregularity, obesity and androgenic effect.)

N.B. Remember the following:

- Antihistamines and other treatments used for angioedema are of limited benefit in hereditary angioedema.
- *Helicobacter pylori* can trigger abdominal attacks. Antibiotics to treat *H. pylori* will decrease abdominal attacks.

Deep Venous Thrombosis (DVT)

Usual instructions are:

- Examine the lower limbs.
- Perform general examination.



Deep venous thrombosis (left lower limb)

Presentation of a Case

- The leg is swollen up to the knee, red or cyanotic, warm with pitting oedema.
- Tenderness in the calf muscles.
- Superficial veins are prominent and tender.
- Homan sign is positive.

Q: What are the differential diagnoses?

A: As follows:

- Cellulitis.
- DVT.
- Ruptured Baker cyst.
- Post-traumatic and calf haematoma.

Q: What is **Homans sign**?

A: Dorsiflexion of foot causes pain in calf muscle (unreliable sign). This test is dangerous because of risk of pulmonary embolism. It is also positive in ruptured Baker cyst, trauma and inflammation in calf muscle.

Q: What are the **common sites** of DVT?

A: Calf muscle veins, popliteal, femoral and iliac veins (swelling up to thigh, femoral or iliac vein thrombosis).

Q: What are the **causes** of DVT?

A: Causes are (**Virchow's law**):

- Stasis.
- Vascular damage.
- Hypercoagulability.

Stasis (which may be due to):

- Prolonged bed rest or immobilisation [after acute myocardial infarction (MI), cerebrovascular accident (CVA) and fracture].
- Postoperative (prostatectomy, hip or pelvic surgery, and lower limbs surgery).
- Pregnancy and puerperium.

Vascular damage (which may be due to):

- Surgery (commonly after prostatectomy, and abdominal and pelvic surgery).
- Trauma.
- Varicose vein.
- Buerger disease.
- Raynaud disease.

Hypercoagulability (which may be due to):

- Oral contraceptive pill.
- SLE (antiphospholipid syndrome).
- Nephrotic syndrome.
- Haematological disease (polycythaemia rubra vera, paroxysmal nocturnal haemoglobinuria, myelofibrosis, essential thrombocythaemia, DIC).
- Internal malignancy (pancreas, lung, ovary and stomach).
- Anticoagulant deficiency (antithrombin III, proteins C and S, factor II or V Leiden).
- Septicaemia.

Q: What are the causes of **recurrent** DVT?

A: As follows:

- Antiphospholipid antibody syndrome, SLE.
- Protein S, C, antithrombin III deficiency.
- Factor V Leiden.
- Polycythaemia rubra vera.
- Oral contraceptive pill use.
- Malignancy.

Q: What **history** should be taken in a patient with DVT?

A: As follows:

- Onset: Acute, chronic or recurrent.
- History of immobilization: Prolonged bed rest, trauma, surgery, CVD, etc.
- History of air travel.
- Drug history (OCP).
- History of any primary disease like polycythaemia rubra vera, malignancy, SLE, nephrotic syndrome, etc.
- Family history.

Q: How to **diagnose** DVT?

A: As follows:

- Doppler USG of lower limb vessels (to note velocity of blood flow in the vein).
- By imaging deep vein with B-mode USG (duplex), thrombosis can be seen.
- D-dimer (high).
- Venography (confirmatory).

N.B. Elevated D-dimer level has a limited diagnostic value since it may be high in other conditions like pulmonary embolism, MI, pneumonia, sepsis, etc. However, a low D-dimer (<500 ng/mL) may be useful in excluding DVT in low-risk patients, and further tests will be unnecessary. In a high-risk patient, D-dimer is less important; and other investigations should be done regardless of the D-dimer value.

Q: What **other investigations** should be done to find out cause?

A: As follows:

- CBC, ESR (may be evidence of polycythaemia rubra vera, SLE).
- Antithrombin III, protein C or S.
- Factor V Leiden level.
- ANA, anti-ds-DNA, antiphospholipid antibody.
- Homocysteine level.
- X-ray chest
- USG of whole abdomen

Q: What are the **complications** of DVT?

A: As follows:

- Pulmonary embolism (commonly from thrombosis in ileo-femoral vein, less commonly from below-knee thrombosis).
- Venous gangrene.
- Postphlebitic syndrome (chronic DVT results in permanently swollen limb with ulceration).

Q: How to **treat** DVT?

A: As follows:

1. General treatment:
 - Bed rest.

- Use of elastic stockings from midfoot to below knee (in calf thrombosis).
- Relief of pain by analgesic.
- Intermittent elevation of foot during day and night (above the heart level).
- Mobilisation slowly, when the patient is fully anticoagulated.

2. Anticoagulation: All patients with above-knee thrombosis must be anticoagulated (as there is more chance of pulmonary embolism). Patients with below-knee DVT should be anticoagulated for 6 weeks.
3. If anticoagulation is contraindicated or with recurrent pulmonary embolism, IVC filter should be given.

Anticoagulant is used as follows:

- Standard unfractionated heparin, initially a loading dose of 5000 IU intravenously, followed by continuous infusion of 1000–2000 IU/hour (20 IU/kg/hour), with infusion pump. APTT monitoring is essential (APTT should be 1.5–2.5 times of control). Heparin should be given at least for 5 days.
- Low-molecular-weight heparin such as enoxaparin is **preferred** (1.5 mg/kg daily subcutaneously).
- Oral anticoagulant (warfarin) should be started with heparin (oral anticoagulant may take 48 h for its full effect). Then heparin may be stopped.

N.B. Warfarin is given 10 mg daily for 2 days. It is followed by a maintenance dose of 3–9 mg, according to international normalized ratio (INR) (target INR should be 2.5). If there is only single episode of thromboembolism, it should be continued for at least 3 months. However, if a definite cause is found and treated, then 4–6 weeks of warfarin may be sufficient. If no cause is found or permanent risk factors are present, it should be continued for 6 months. In recurrent cases, it should be continued for longer time, even life long.

Q: Why low-molecular-weight heparin is **preferred**?

A: It has the following advantages:

- Does not affect APTT (no need of frequent APTT testing).
- Long half-life (may be given in single dose daily).
- High bioavailability.
- Greater activity against factor Xa.
- Can be given in a fixed dose.
- Less inhibition of platelet (standard heparin can cause thrombocytopaenia).

Q: What is the **mode of action** of heparin?

A: Heparin acts by potentiating the activity of antithrombin, which inhibits procoagulant enzyme activity of factors IIa, VIIa, IXa, Xa and XIa.

Q: What are the **complications** of long-term heparin use?

A: As follows:

- Osteoporosis.
- Thrombocytopaenia (if heparin is used for more than 7–10 days).
- Hyperkalaemia (if heparin is used for more than 7 days).

Q: What is the **antidote** of heparin?

A: Protamine sulphate.

Q: What is the mode of **action** of warfarin?

A: Inhibit vitamin K-dependent factors (II, VII, IX and X).

Q: What is the **antidote** of warfarin?

A: Vitamin K.

N.B. After warfarin therapy, if INR is high, above the desired, withhold or reduce the dose. If INR is more than 8, then start with vitamin K, 2 mg IV slowly or 5 mg orally. In case of severe bleeding, concentrate factor containing II, III, IX and X, or fresh frozen plasma may be given.

Q: What are **thrombophlebitis** and **phlebothrombosis**?

A: **Thrombophlebitis** (superficial vein thrombosis): Inflammation involving superficial veins (after intravenous fluid or in varicose vein). It is characterised by:

- Pain—the main feature.
- Increased local temperature.
- Skin is inflamed.
- Vein, prominent superficial vein, hard and tender.
- Thrombosis is attached to the vein. Hence, there is less chance of pulmonary embolism than phlebothrombosis.

Phlebothrombosis (DVT): Thrombosis in deep veins is noninflammatory in nature. It is characterised by:

- Pain and swelling of the leg.
- It is in the deeper vein, mostly asymptomatic.
- No inflammation.
- There is more chance of pulmonary embolism than thrombophlebitis.

Q: How to prevent DVT?

A: As follows:

- Early mobilisation.
- Leg exercise.
- Elastic stockings.
- Low-dose aspirin.
- Low-molecular-weight heparin should be given following surgery or acute MI (enoxaparin 40 mg S/C daily).
- Avoid oral contraceptive pill.
- Treat the primary cause.



Deep venous thrombosis (left)

Cellulitis and Erysipelas

Cellulitis

Usual instructions:

- Examine the lower limbs.
- Look at here. What is your diagnosis?

Presentation of a Case

- There is erythematous and darkly pigmented area involving the dorsum of left foot extending up to the lower part of leg.
- There are multiple vesicles or blisters or crusts.
- Local temperature is raised and the part is also tender.

Diagnosis is **cellulitis.**



Cellulitis (dorsum)



Cellulitis—side of leg (with blister)

Q: What is cellulitis? What are the causative organisms?

A: It is the acute spreading inflammation of skin and subcutaneous tissue with local pain, swelling and erythema. It may be secondary to infection in surgery, burn or fungal infection in feet or toe.

Causes: Commonly due to the infection of group A *Streptococcus pyogenes*; also because of *Staphylococcus aureus*. In immunosuppressed or diabetic patients, Gram-negative organisms or anaerobes should be suspected.

Skin on the face or lower legs (shin and ankle) are commonly affected by this infection; though cellulitis can occur in any part of the body. It appears as a swollen, red area of the skin, which is hot and tender, and may spread rapidly. It left untreated, the spreading infection may rapidly turn into life-threatening condition.

Treatment: Antibiotic (phenoxymethyl penicillin, erythromycin, flucloxacillin or cephalexin). In severe cases, intravenous therapy followed by oral therapy is given. If there is recurrent cellulitis, low-dose antibiotic prophylaxis with phenoxymethylpenicillin 500 mg twice daily should be given.

Q: What are the **differential diagnoses** of cellulitis?

A: As follows:

- DVT.
- Trauma.
- Acute arthritis.
- Ruptured Baker cyst.

Erysipelas

Q: What is **erysipelas**? What are the **causes** and **risk factors**?

A: It is an acute, superficial form of cellulitis, which occurs classically in the cheek, but may occur in other parts of the skin as well, caused by *Streptococcus* β-haemolyticus. The infection involves dermis and lymphatics, and is more superficial subcutaneous infection than cellulitis.

Causes: Most common cause is group A streptococcus; less common are group G, C and B streptococci. Staphylococcal infection is rare.

Risk factors: Elderly, infants, children, diabetes mellitus, alcoholism, immunodeficiency, lymphatic obstruction, etc.



Erysipelas

Clinical features:

- Erysipelas is characterised by rapidly enlarging erythematous skin lesion that commonly involves the face, but may also occur on limbs and trunk. The lesion is red, swollen, warm, indurated and painful. The margin is raised and has a sharply demarcated border (differentiating it from other skin infection).
- In severe cases, there may be vesicles, blisters and even skin necrosis. There may be marked oedema, with eyes closed.
- LN draining the area is enlarged and tender. Occasionally, a red streak extending to the LN can be seen.
- There are usually systemic features like high fever, shaking, chills, fatigue, arthralgia, etc.

N.B. In erysipelas, pustule and gangrene are usually absent. It heals without scar.

Differential diagnoses:

- Cellulitis
- Contact dermatitis.
- Angioedema.
- Herpes zoster.
- Diffuse inflammatory carcinoma of the breast.

Treatment: Antibiotics (such as penicillin, clindamycin, erythromycin)—oral or intravenous.

Complications:

- Septicaemia leading to septic arthritis.
- Glomerulonephritis.
- Necrotizing fasciitis.
- Recurrent infection.
- Lymphatic damage.

Peripheral Vascular Disease

Usual instructions are:

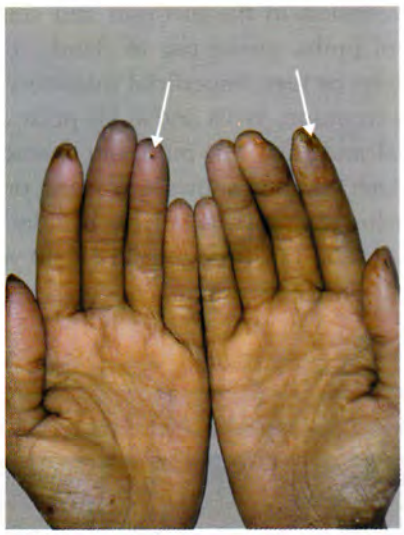
- Examine the leg or perform the general examination of this patient.

Presentation of a Case

- The right leg and foot is pale, and the toes are bluish red.
- There is wasting of right leg with prominent veins.
- Skin is shiny with loss of hairs.
- Local temperature is reduced.
- There is an ulcer at the tip of great toe and sole of right foot.
- Pulse is absent in arteria dorsalis pedis and reduced in posterior tibial.
- No femoral bruit.
- No sensory abnormality.
- Reduced capillary return (press the nail and note the return of normal red colour, which is slow).

My diagnosis is **peripheral vascular disease,** more likely Buerger disease (in young patient). If the patient is elderly, likely diagnosis is peripheral vascular disease due to atherosclerosis.





Raynaud disease (gangrene of the tip of fingers)



Buerger disease (amputation of great toe)



Buerger disease (gangrene of the tip of toes)

Q: Ask **one question** to the patient.

A: Ask about smoking habit, with number of sticks and duration.

Q: Ask **another question.**

A: History of intermittent claudication; also claudication distance.

Q: What **bedside test** should be done in Buerger disease?

A: Buerger test: Elevate the limb at 45°—there is pallor and patient may complain of pain. Then, the patient sits with the feet hanging lower to the ground for 2–3 minutes. There is cyanotic hue in the affected foot (Buerger sign).

Q: What are the **differential diagnoses?**

A: As follows:

- Raynaud disease: More in female, and commonly involves the upper limb. History such as exposure to cold will produce typical colour change (see page 386). Buerger disease itself can cause Raynaud phenomenon.
- Atherosclerosis: Common in the elderly. There may be bruit over femoral artery. It may be present in young, if associated with hypercholesterolaemia. Look for corneal arcus, tendon xanthoma, palmar xanthoma and xanthelasma.
- Vasculitis due to any cause.
- Takayasu disease.

Q: What are the **risk factors** for peripheral vascular disease?

A: Mostly, these are the risk factor for atherosclerosis:

- Family history of heart attacks or strokes.
- Age >50 years.
- Smoking.

- Diabetes mellitus.
- Hypertension.
- Obesity.
- Sedentary lifestyle.
- Dyslipidaemia.

Q: What **investigation** should be done for peripheral vascular disease?

A: As follows:

- CBC, ESR.
- CRP.
- Urine R/M/E (haematuria)
- Chest X-ray (pulmonary infiltrate is Wegener granulomatosis, PAN).
- X-ray of the involved area: May show calcification of the arteries.
- Serum lipid profile.
- pANCA and cANCA, ANA, anti-ds-DNA.
- Doppler study of the lower limb vessels.
- Arteriography may be needed in some cases.

Q: How to **treat** the peripheral vascular disease?

A: As follows:

1. General measures: Smoking should be stopped, reduction of weight, if obese, regular exercise, limb should be kept warm but avoid local heat, local care of foot, use of appropriate footwear, etc.
2. Medical treatment:
 - Treatment of any risk factors like diabetes mellitus, hypertension, dyslipidaemia.
 - Antiplatelet agent (aspirin 75 mg daily or clopidogrel 75 mg daily)
 - Pentoxifylline: It improves blood flow by decreasing the viscosity of blood and making red blood cells more flexible.
 - Cilostazol: It prevents clumping of platelets. It also helps dilate the blood vessels, encouraging the flow of blood.
3. Surgical:
 - Percutaneous transluminal angioplasty, stenting, endarterectomy or bypass graft.
 - Sometimes sympathectomy may be needed.
 - Amputation may be necessary in case of gangrene.

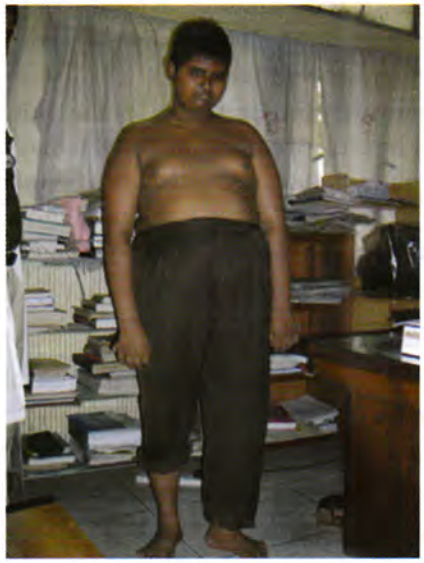
Buerger Disease

It is an inflammatory, obliterative, arterial disease with proliferative lesion in the medium and small arteries and veins of limbs, giving rise to claudication or rest pain in fingers or toes. Superficial migratory thrombophlebitis is common. Wrist and ankle pulse are absent, but brachial and popliteal pulse are characteristically palpable. Arteriography shows narrowing or occlusion of artery below the knee, relatively healthy above the knee. It is common in young male, 20–40 years of age and in moderate to heavy smokers.

Laurence–Moon–Bardet–Biedl Syndrome

Usual instruction:

- Perform the general examination.



Obesity and short stature



Polydactyly (six toes)



Gynaecomastia with polydactyly (six fingers)



Polydactyly (six fingers)

Presentation of a Case

- The patient is obese, looks short.
- There is polydactyly (one extra finger in each hand and one extra toe in each foot).

Diagnosis is **Laurence–Moon–Bardet–Biedl syndrome.**

Q: What **else** do you like to see?

A: Signs of hypogonadism and fundoscopy to see retinitis pigmentosa.

Q: What is **Laurence–Moon–Bardet–Biedl syndrome?**

A: It is an autosomal recessive disorder, characterised by:

- Obesity.
- Short stature (not always).
- Mental retardation.
- Polydactyly.
- Hypogonadism (gynaecomastia and small testis).
- Retinitis pigmentosa.

Hypogonadism, mental retardation and polydactyly are less frequently found in females. Renal structural and functional abnormalities are very common. Interstitial nephritis may lead to renal failure.

Generalized Oedema

Presentation of a Case

- There is generalized oedema (also called anasarca) involving the whole body, which is pitting.



Generalized oedema in nephrotic syndrome

My **differential diagnoses** are (causes of generalized oedema):

- Nephrotic syndrome.
- Hypoproteinaemia due to any cause
- Hypothyroidism (nonpitting).
- CKD (in advanced stage).
- Decompensated cirrhosis of liver (advanced stage).
- Congestive heart failure (advanced stage).

Q: How can you differentiate oedema of cardiac, renal and liver disease clinically?

A: As follows:

- CCF: Oedema is usually dependant, mostly in the leg. Other features are engorged and pulsatile neck vein, enlarged tender liver. Evidence of cardiac disease is usually present.
- Nephrotic syndrome: Oedema usually starts from the face or periorbital, then descents, later becomes generalized. Urine shows massive proteinuria.
- AGN: Oedema is periorbital, associated with scanty, froathy, smokey micturition.
- Chronic kidney disease: Previous history of renal disease or hypertension, DM are usually present. Other features of CKD are present.
- Cirrhosis of liver: Usually there is ascites, later in advanced stage there may be generalized oedema.

Q: What is **oedema?** What are the **types?**

A: It may be defined as excessive accumulation of fluid in the interstitial space. It may be pitting and nonpitting.

Q: What are the causes of **pitting** oedema?

A: As follows:

- CCF.
- Nephrotic syndrome
- Hypoproteinaemia due to any other cause (protein loosing enteropathy or less protein intake).
- Deep venous thrombosis.
- Compression of large veins by tumour or lymph nodes.

- Chronic venous insufficiency (varicose vein).
- Drugs (calcium channel blockers [e.g. nifedipine, amlodipine], some NSAIDs).
- Idiopathic (also called 'fluid retention syndrome', common in women).

Q: What are the causes of **nonpitting** limb oedema?

A: As follows:

1. Myxoedema.
2. Chronic lymphatic obstruction or lymphoedema due to any cause (see below).

Q: What are the causes of **periorbital oedema or puffiness?**

A: As follows:

- Nephrotic syndrome
- AGN
- Myxoedema
- Angioneurotic oedema
- Surgical emphysema
- Orbital cellulitis
- Malignant exophthalmos (in Graves disease)
- Dermatomyositis

Q: How will you investigate a patient with generalized oedema?

A: Investigation should be according to history, physical finding and suspicion of cause.

- Nephrotic syndrome: Urine R/E, blood for total protein, 24 hour urinary protein
- CCF: Chest X-ray, ECG, echocardiogram
- Cirrhosis of liver: LFT (total protein, A:G ratio, prothrombin time, ultrasonography etc)
- Hypoproteinaemia: Serum total protein, other investigation according to the history to find out cause.
- Hypothyroidism: FT_3, FT_4, TSH.

Tongue

Presentation of Case No. 1

- The tongue is pale, smooth and shiny with atrophy of papillae.



Smooth pale tongue

My differential diagnoses are:

- Iron-deficiency anaemia.
- Vitamin B_{12}-deficiency anaemia.
- Riboflavin deficiency.

Presentation of Case No. 2

- There are multiple white patches over the surface of the tongue with some denuded area on the margin.



Oral candidiasis



Oral candidiasis

My diagnosis is **oral candidiasis.**

Q: What are the **underlying diseases** associated with oral candidiasis?

A: As follows:

- Poor oral hygiene.
- Diabetes mellitus.

- Immunosuppressive disease, e.g. lymphoma, leukaemia, malignancy, HIV.
- Prolonged use of antibiotics, steroids and immunosuppressive drugs.
- Steroid inhaler use.

Q: What is the **typical finding** in mouth in HIV?

A: Hairy leukoplakia (commonly on the lateral margin of tongue).

Q: How would you **treat** oral candidiasis?

A: As follows:

- Topical antifungal: Nystatin, econazole, miconazole.
- Systemic antifungal: Fluconazole, clotrimazole, etc.
- Maintenance of oral hygiene; antiseptic mouthwash may be used.
- Treatment of the underlying disease.

Q: What is **disseminated** candidiasis?

A: It is characterized by fever, pulmonary involvement, retinal abscess, endocarditis, skin abscess, brain abscess, osteomyelitis, etc. Intravenous amphotericin B may be used in such cases.

Presentation of Case No. 3

- The tongue is black and rough with pale margin.



Black hairy tongue

My diagnosis is black hairy tongue.

Q: What are the **causes**?

A: Causes are poor oral hygiene, prolonged use of antibiotics, steroids, oral contraceptive pill, bismuth, smoking, mouth breathing, radiotherapy etc. It is usually a benign condition.

Q: What **diagnoses** are possible by looking at the tongue?

A: As follows:

1. Dry or moist:
 - Dry: Dehydration, mouth breathing, xerostomia (in Sjogren syndrome), anticholinergic drug therapy.
 - Moist: Sialorrhoea in postencephalitic Parkinsonism, local mouth infection, gastroesophageal reflux disease (GERD), heavy metal poisoning.
2. Colour:
 - Pale: Anaemia.
 - Yellow: Jaundice (mainly in undersurface of tongue).
 - Bluish: Central cyanosis, methaemoglobinaemia, sulphaemoglobinaemia (mainly involves the sides of the tongue), blue coloured food material.
 - Bluish red: Polycythaemia.
 - Black tongue (lingua nigra): Ingestion of bismuth, liquorice, charcoal, etc., Addison disease (pigmented).
 - Brownish: CKD.
 - Magenta coloured: Riboflavin (vitamin B_2) deficiency.
 - Raw beefy tongue (red, swollen and painful): Vitamin B_{12} deficiency, niacin deficiency (pellagra).
 - White patches over tongue: Candidiasis, leukoplakia, chronic superficial glossitis.
 - Black hairy tongue: Smoking, fungal infection, tetracycline, penicillins.
 - White or greyish coating or "furred tongue": Smoking, chronic debilitating disease.
 - White and red strawberry tongue: Scarlet fever.
 - Geographical tongue (there are irregular red and white patches on the tongue. These lesions look like a geographic map. Slowly changing red rings and lines that occur on the surface of the tongue). It has no clinical significance, but, can be a sign of riboflavin deficiency.
 - Scrotal tongue (deep horizontal fissure): No clinical significance.
 - Mushroom-like tongue (sore tongue with white slough): Corrosive poisoning.
 - Blotting paper-like pallor with black pigmentation in the margin: Hook worm infestation.
 - Angry looking tongue (central coating with red tip and margins): Enteric fever.
 - Glossitis or bald tongue (total loss or atrophy of papillae, smooth tongue): Vitamin B_{12} deficiency, iron-deficiency anaemia, coeliac disease, pellagra, tropical sprue.

3. Mass or ulcers:
 - Ulcers: Aphthous, malignant, tuberculous, snail track ulcer in secondary syphilis, denture, Crohn disease.
 - Bite mark: Convulsion.
 - Growth in tongue: Squamous cell carcinoma.
 - Hairy leukoplakia (painless white corrugated lesion on sides): Found in AIDS due to EBV infection.
 - Papilloma (viral wart).
 - Median rhomboid glossitis (lozenge shaped area with loss of papillae and fissuring in the midline of the tongue, anterior to the foramen caecum). It is a congenital anomaly.
 - Cysts in the floor of the mouth: Ranula, sublingual dermoid cyst.
4. Size and shape:
 - Macroglossia: Found in Down syndrome, acromegaly, cretinism, myxoedema, primary amyloidosis, mucopolysaccharidosis (e.g., Hurler syndrome), lymphangioma, tumour infiltration.
 - Microglossia (atrophy or hemiatrophy): Found in bulbar and pseudobulbar palsy, lower motor neuron (LMN) lesion of XIIth cranial nerve.
 - Tongue-tie (ankyloglossia).
 - Acute swelling: Infection, angioneurotic oedema.
5. Neurological disease:
 - Flaccid wasted tongue with fasciculation: Bulbar palsy.
 - Spastic tongue without fasciculation: Pseudobulbar palsy.
 - Jack in the box sign: Rheumatic chorea.
 - Tremor: Anxiety neurosis, thyrotoxicosis, chronic alcoholism, Parkinsonism.
 - Deviation of the tongue: Deviated to the opposite side is due to upper motor lesion of the 12th cranial nerve. Deviated to the same side is due to lower motor lesion of the 12th nerve.
 - Loss of taste sensation: Anterior 2/3rd by facial nerve, posterior 1/3rd by glossopharyngeal nerve. (Site of taste sensation – sweet at the tip, sour at the margin, bitter at the back and salty at any part of the tongue).
 - Fasciculation: Bulbar palsy, LMN palsy of XIIth cranial nerve.
 - Trombone tongue: Rapid forward and backward movement of the tongue, found in general paresis of insane (GPI).
 - Chewing tongue: Found in athetosis

Q: What are the causes of **mouth ulcer?**

A: As follows:

- Aphthous ulcer (usually idiopathic, sometimes premenstrual).
- Trauma.
- GIT disease: Crohn disease, ulcerative colitis, coeliac disease.
- Rheumatological disease: SLE, Behcet syndrome, Reiter syndrome.
- Local infection: Viral (herpes simplex), syphilis (chancre in primary and snail tract ulcer in secondary syphilis), tuberculosis, Vincent angina.
- Stevens–Johnson syndrome.
- Pemphigus vulgaris, pemphigoid.
- Erosive lichen planus.
- Cytotoxic drugs.

Q: What are the **sign and symptoms of oral cancer?**

A: As follows:

- Single ulcer (without local trauma).
- Single white patch ('leukoplakia').
- Single red patch.
- Fixed mass.
- Cervical lymphadenopathy.

Q: What are the causes of **halitosis** (bad breath)?

A: As follows:

- Poor oral hygiene.
- Fetor hepaticus (like dead mouse. It is due to methyl mercaptan, found in hepatic precoma).
- Acetone breath (present in diabetic ketoacidosis).
- Fishy ammoniacal (present in renal failure).
- Others: Smoking, alcoholism, lung abscess (foetid), bronchiectasis, Zenker diverticulum, offensive faecal smell in gastrocolic fistula.

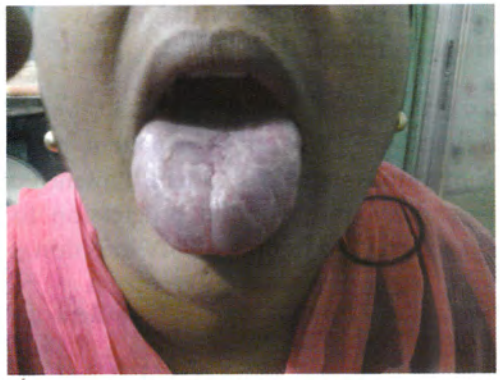
Q: What are the causes of **gum hypertrophy?**

A: As follows:

- Pregnancy.
- Drug: Phenytoin, nifedipine, ciclosporin, oral contraceptive pill with high oestrogen.
- Acute leukaemia (mainly myelomonocytic leukaemia).
- Gingivitis.
- Scurvy.



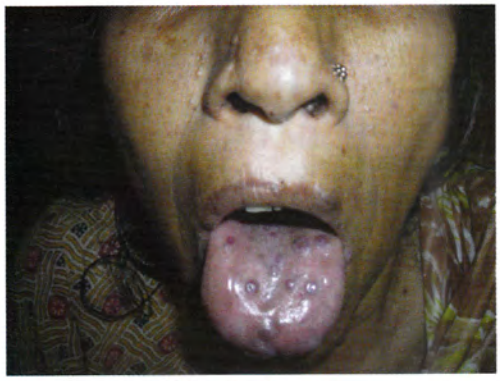
Black tongue



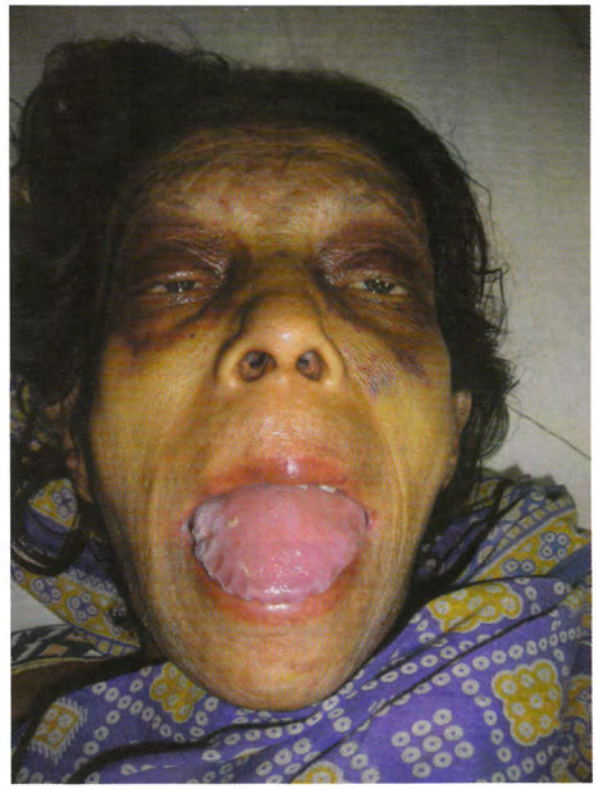
Geographical tongue



Gum hypertrophy with oral candidiasis



Haemangiaoma



Macroglossia



Oral lichen planus



Raw beefy tongue



Spirit ingestion



Stevens–Johnson syndrome

Hairy Leukoplakia

Usual instruction:

- Examine the mouth or look at the tongue.

Presentation of a Case

- There are white, slightly raised, corrugated, irregular, hairy lesions on the margin of the tongue with few furring.



Hariy leukoplakia

My diagnosis is **hairy leukoplakia**.

Q: What is your **differential diagnosis**?
A: Oral candidiasis and lichen planus.

Q: What is the **difference** between hairy leukoplakia and oral candidiasis?
A: Oral candidiasis can be rubbed off and respond to local and systemic antifungal therapy. Hairy leukoplakia cannot be rubbed off and do not respond to antifungals.

Q: What is the **cause** of hairy leukoplakia?
A: Epstein–Barr virus.

Q: What is the **underlying** disease?
A: It is found in HIV seropositive patient, rare in non-HIV immunosuppressed patient. Presence of hairy leukoplakia indicates rapid progression to AIDS. It may be an early finding of HIV infection.

Q: What is the common **site** of hairy leukoplakia in tongue?
A: It usually involves the lateral border of the tongue.

Q: What is the **treatment**?
A: Zidovudine or acyclovir may be helpful. Podophyllin and retinoid may be used.

Q: Can it become **malignant**?
A: No, it is not premalignant.

Q: What is **leukoplakia**?
A: It is the white thickening of the tongue or oral mucosa of unknown cause. It is premalignant. It may be associated with alcohol and smoking. Biopsy should always be taken. Treatment is unsatisfactory; isotretinoin may be used.

Q: What are the causes of **white intraoral lesion**?
A: As follows:

- Candidiasis.
- Leukoplakia.
- Hairy leukoplakia.
- Lichen planus.
- SLE.

- Smoking.
- Poor dental hygiene.
- Aphthous ulcer.
- Squamous papilloma.
- Secondary syphilis.
- Carcinoma.
- Idiopathic keratosis.

Q: What are the **premalignant** oral lesions?

A: As follows:

- Leukoplakia.
- Lichen planus.
- Erythroplakia (red patches).
- Submucous fibrosis.

Dupuytren Contracture

Presentation of a Case

- There is thickening of the palmar fascia, more marked along the ulnar side with flexion contracture of 4th and 5th fingers of both hands (may be all the fingers).

My diagnosis is **Dupuytren contracture**.

Q: What is your **differential** diagnosis?

A: Diabetic cheiroarthropathy.

Q: What is **Dupuytren contracture**? What are **the causes**?

A: It is characterized by thickening, fibrosis and shortening of superficial palmar fascia, causing flexion contracture of fingers. The ring and little fingers are commonly affected.

In Dupuytren contracture, there is inability to extend the fingers, puckering of the skin and presence of palpable nodules; it may affect the sole of foot. It is usually painless and often bilateral, more common after 40 years, but increases in incidence with advancing age. Five times common in male than female; it may be familial with dominant inheritance. It is more common in Whites and Europeans.

Mechanism is unknown. Palmar fascia contains large amount of xanthine, which may be related to the pathogenesis.

Causes of Dupuytren contracture:

- Cirrhosis of liver (commonly alcoholic).
- Alcoholism (itself, not necessarily by cirrhosis).
- Prolonged use of antiepileptic drug (phenytoin).
- Manual worker (gardener) and chronic vibration injury.
- Traumatic.
- Familial (as autosomal dominant, associated with Garrod patch on dorsum of hand).
- Diabetes mellitus (diabetic cheiroarthropathy, confuses with systemic sclerosis).
- May be associated with tuberculosis.
- Retroperitoneal fibrosis.
- Peyronie disease.
- Idiopathic (in many cases).

Q: How to **treat** Dupuytren contracture?

A: As follows:

- Exercises, warm water application or splints may be helpful.
- If the palmar thickening is growing rapidly, triamcinolone may be injected into the growing nodule.
- Radiation therapy may be used in early stages.
- Surgery: When there is severe flexion contracture. In 50% cases, it may recur within 10 years after surgery.
- New treatment: Injection of collagenase into the scarred or fibrous tissue.

Q: What is the **prognosis** or natural course of Dupuytren contracture?

A: Natural course is unpredictable. It may be slowly progressive with little disability over many years. In some patients, it may progress rapidly with severe deformity and functional disability.

Q: What is **diabetic cheiroarthropathy?**

A: It is a complication of long-standing diabetes mellitus. In this condition, skin of the dorsum of fingers is tight, waxy, shiny, and depigmented with joint stiffness and flexion deformities of many fingers. Usually painless, limitation of joint movement may be present. There is inability to extend the metacarpophalangeal (MCP) or interphalangeal (IP) joint of at least one finger bilaterally. This can be better detected by **prayer sign.** Occasionally, affects the wrist and shoulders. Cause of cheiroarthropathy is unknown, probably there is cross-linking and thickening of collagen. It occurs in any type of diabetes mellitus, and is confused with systemic sclerosis. There is no specific treatment.



Dupuytren contracture



Dupuytren contracture

Paget Disease

Presentation of Case No. 1

- This elderly man has asymmetrical enlargement of skull, more on the right.
- Right side of the face is also enlarged.



Asymmetrical enlargement of skull.

My diagnosis is **Paget disease**.

Q: What **else** do you like to see in this patient?

A: As follows:

- Bone in other parts of the body: Leg (bowing of tibia), spine (kyphosis), any other bone enlargement.
- Local warmth.
- Hearing (deafness).
- Heart (there may be evidence of high-output cardiac failure).
- Fundoscopy (to see optic atrophy and angioid streaks in retina).

Presentation of Case No. 2

- This elderly man has bowing of both tibias, more on the right side.



Bowing of tibias.

My diagnosis is **Paget disease**.

Q: What are the causes of **bowing of tibia**?

A: As follows:

- Paget disease.
- Rickets.
- Congenital syphilis (sabre shin).

Q: What is **Paget** disease (osteitis deformans)? What are the **features**?

A: Paget disease is characterized by excessive and disorganized resorption and formation of bone, resulting in deformity and fracture. Commonly involved bones are pelvis, femur, tibia, lumbar spines, skull and scapula. Common over 55 years of age, is rare under 40 years. More in temperate climate; male and female ratio is 2:3.

In Paget disease, there is increased osteoclastic bone resorption and increased osteoblastic activity followed by abnormal bone formation. Bone formation exceeds resorption; the new bone is bigger, but weaker and filled with new blood vessels. The disease may involve one bone (monostotic, 10–15%) or many bones (polyostotic).

Features are:

- Many cases are asymptomatic (60–80%), detected radiologically.
- There may be bone pain, joint pain or stiffness, bowing of the legs, deformities (in weight-bearing bones such as femur, tibia), pathological fracture, enlarged head and other visible features.
- Neurological features such as deafness, cranial nerve defect, nerve root pain, spinal cord compression and spinal stenosis may occur due to enlargement of affected bone.
- Warm skin over the affected bone, high-output cardiac failure due to hyperdynamic circulation (due to increased vascularity of the bone), etc.

Cause is unknown. Genetic factors are important. Some slow viruses like measles may be involved.

Q: What **investigations** should be done?

A: As follows:

- Bone X-ray: Enlargement of bone with typical lytic and sclerotic lesion. X-ray skull shows lytic lesion osteoporosis circumscripta, also enlargement and sclerosis, thickening of trabeculae.
- Serum alkaline phosphates (Usually high; may be normal in 10% cases due to monostotic involvement).
- Isotope bone scan (to see extent of bone involvement. It cannot differentiate between Paget disease and osteoblastic metastatic carcinoma).
- Urinary hydroxyproline (high; it is a marker of bone breakdown).
- CT scan or MRI of bone may be done.
- Rarely bone biopsy.
- Calcium and phosphate: Normal (calcium may be high in prolonged immobilization or fracture).

Q: How to **treat** Paget disease?

A: As follows:

1. For pain: NSAIDs
2. To prevent further bone break down:
 - Bisphosphonates: Pamidronate, zoledronate, risedronate are more effective. Also etidronate and tiludronate. (Hypocalcaemia may occur, so adequate calcium and vitamin D should be taken.)
 - Calcitonin: May be used subcutaneously 100–200 IU, three times weekly, for 2–3 months. It is less convenient and more expensive.
3. Orthopaedic surgery: Joint replacement or osteotomy may be needed. Neurosurgery may be needed in spinal cord compression.

Q: What are the **complications** of Paget disease?

A: As follows:

- Bone fractures and deformities.
- Deafness due to otosclerosis of the ossicles, less due to compression of VIIIth cranial nerve.
- High-output heart failure.
- Secondary osteoarthrosis.
- Optic atrophy.
- Spinal cord compression causing paraplegia.
- Spinal stenosis.
- Basilar invagination (platybasia) causing brainstem sign.
- Osteosarcoma (Rare but serious. Occurs in 1% in those for >10 years).

Examination of Hands

The usual instructions are:

- Look at the hands. What is the diagnosis?
- Examine the hands.

By looking, the obvious findings may be:

- Rheumatoid arthritis (to examine rheumatoid hand, see in the Chapter 9).
- Systemic sclerosis (see in the Chapter 9).
- Tophaceous gout.
- Bouchard nodes, Heberden node (in osteoarthritis).
- Skin rash and Gottron patch (dermatomyositis).
- Large size (acromegaly).
- Claw hand.

- Wrist drop.
- Myotonic dystrophy (diagnosed by handshake or asking the patient to close and open the hands).
- Raynaud disease or phenomenon.
- Arachnodactyly.
- Syndactyly.
- Polydactyly.
- Short 4th metacarpal.
- Palmar erythema.
- Nail and nail bed change: Clubbing, koilonychia, leukonychia, half-and-half nail, splinter haemorrhage (infective endocarditis), Beau line, Mee line, nail fold telangiectasia and erythema (SLE), fungal infection, periungual fibroma, nail pitting (psoriatic arthritis), yellow nail syndrome, absent nail (nail patella syndrome), onycholysis, nicotine stain.
- Dupuytren contracture.
- Trophic change (gangrene, ulceration).
- Wasting: Thenar, hypothenar or generalized.
- Tremor.
- Warm and sweaty palm (thyrotoxicosis), cold and sweaty palms (anxiety).
- Single palmar crease (in Down syndrome).

If it is RA or systemic sclerosis, then follow the examination accordingly.

If wasting is obvious, see the site—generalised or localized (thenar or hypothenar):

- If there is thenar wasting only: It indicates median nerve lesion.
- If there is appearance of hypothenar and other muscles wasting (except thenar): Indicates ulnar nerve lesion.
- On the dorsum: Wasting with dorsal guttering (interossei) indicates ulnar nerve lesion.
- Generalised wasting indicates C8 and T1 lesion.

Then, perform the **neurological** examination as follows:

1. Sensory tests in the sensory supply along ulnar and median nerve [(if wasting is present, but sensory is intact, more likely diagnosis is motor neurone disease (MND)].
2. Next, perform the motor function of hand muscles (ask as follows):
 - 'Open and close the hands as quickly as possible' (observe the weakness and evidence of myotonia dystrophica).
 - 'Point your thumb towards the ceiling and stop me from bending it' (test for abductor pollicis brevis).
 - 'Fix the tip of little finger and thumb, and stop me from separating it' (test for opponens pollicis).
 - 'Spread your fingers wide apart and stop me pushing them together' [test for dorsal interossei **(DAB)** means dorsal abduction].
 - 'Hold a piece of paper between two fingers and stop me from taking it out' [test for palmar interossei **(PAD)** means palmar adduction].
 - 'Hold a paper between thumb and index finger and stop me from taking it out' [test for adductor pollicis]. If the muscle is paralysed, the patient can hold the paper by flexing thumb. It is called **Froment sign.** (It indicates ulnar nerve lesion.)
 - 'Squeeze my fingers' (test for C8 and T1 lesion), long and short flexors of the fingers.

Q: What are the findings in hand in **infective endocarditis?**

A: As follows:

- Osler nodes (small painful violaceous raised nodule, 0.5–1.5 cm, present on the tip of the fingers and toes, also palmar aspect, probably due to development of vasculitis or septic emboli).
- Splinter haemorrhage.
- Clubbing.
- Janeway lesion (large painless erythematous macule containing bacteria on palm, pulp of the fingers. It may be found in the sole).
- Petechial haemorrhage.
- Infarction on the tip of the fingers.

Q: What are the findings in hand in **CLD?**

A: As follows:

- Palmar erythema.
- Dupuytren contracture.
- Clubbing.
- Leukonychia.
- Flapping tremor.
- Spider angioma.
- Pigmentation.
- Jaundice.
- Scratch mark.
- Xanthoma.
- Cyanosis.



Arachnodactyly



Dupuytren contracture with palmar erythema



Clubbing with Beau line



Heberden node



Clubbing with leukonychia



Koilonychias



Digital infarction in peripheral arterial disease



Myotonic dystrophy



Myotonic dystrophy



Osler lesion in SBE



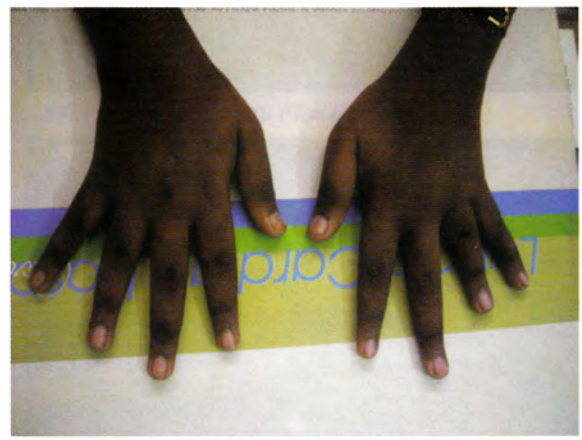
Polydactyly



Rheumatoid hand



Prayer sign



Short 4th metacarpal of the left hand



Single palmar crease in Down syndrome



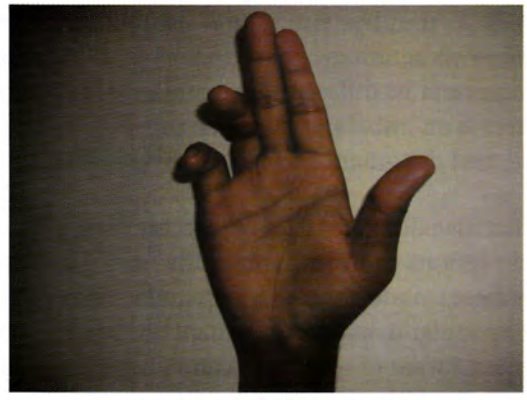
Splinter haemorrhage



Systemic sclerosis



Syndactyly in left hand with one extra finger



Ulnar claw hand



Syndactyly in right index and middle fingers



Wasting of thenar and hypothenar muscles

Lupus Pernio

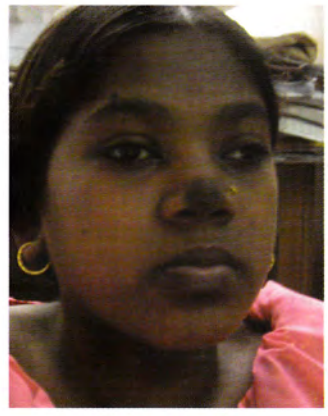
Usual instruction:

- Look at the patient's face. Or perform the general examination.

Presentation of a Case:

- There is bluish (or violaceous) discoloration at the tip and ala of the nose.

My diagnosis is **lupus pernio**.



Lupus pernio.

Q: What are the **sites** of lupus pernio?
A: Nose, cheeks, earlobes, hands and feet.

Q: What is the **underlying disease**?
A: It is due to sarcoidosis. It indicates chronic pulmonary sarcoidosis (may progress to fibrosis of lung; also chronic uveitis and bone cyst in the phalanges may be present).

Q: What is the **differential diagnosis** of lupus pernio?
A: SLE, rosacea, rhinophyma, lupus vulgaris, leprosy.

Q: What is **sarcoidosis**? What are the causes?
A: It is a multisystem granulomatous disease of unknown aetiology, characterized by noncaseating granuloma in different organs. Cause is unknown. There is an imbalance between subset of T lymphocyte and disturbance of cell-mediated immunity.

Q: What **else** do you want to see in sarcoidosis?
A: Skin lesions in other parts of the body like plaque, erythema nodosum, maculopapular lesion, hyper- or hypopigmentation, subcutaneous nodule, etc.

Also, I want to see other features of sarcoidosis like generalized lymphadenopathy, hepatosplenomegaly, lung (to see evidence of fibrosis), eyes (uveitis), bilateral parotid involvement, neurological examination (to see evidence of neurosarcoid), etc.

Q: What **history** do you like to take?
A: Fever, arthritis, arthralgia, cough or breathlessness, etc.

Q: How the patient of sarcoidosis usually **presents**?
A: Common in young adult, in 3rd or 4th decade, slightly more in female. Presentation may be:

- Asymptomatic [commonly affecting young adults, usually presents BHL in X-ray chest or abnormal liver function test (LFT)].
- Symptomatic: Fever, polyarthritis or arthralgia, erythema nodosum, other skin lesions such as lupus pernio, plaque, skin rash and other organ involvement.
- Other features: Bilateral parotid enlargement, eye signs (episcleritis, scleritis), cardiac involvement (arrhythmia, cardiomyopathy, cardiac failure), pulmonary involvement, neurological features such as cranial nerve palsy, meningism, seizure, psychosis, diabetes insipidus, etc.

N.B. Presence of fever, arthritis or arthralgia, erythema nodosum plus BHL on x-ray is highly suggestive of sarcoidosis.

Q: What is **Lofgren syndrome**?
A: In sarcoidosis when there is erythema nodosum, polyarthralgia and BHL, it is called Lofgren syndrome.

Q: What is **Heerfordt syndrome** (uveoparotid fever or Heerfordt–Waldenström syndrome)?
A: It is characterized by fever, bilateral parotid enlargement, anterior uveitis and lower motor neuron facial palsy.

Q: What **investigation** should be done?
A: As follows:

1. CBC, ESR (lymphopenia, high ESR).
2. MT (usually negative).
3. Serum calcium and γ-globulin (usually high).
4. X-ray chest (BHL, lung infiltrate, pulmonary fibrosis, honeycomb shadow, miliary mottling, eggshell calcification).
5. X-ray of hands or feet (cyst may be found in the phalanges).
6. X-ray kidney (may show nephrocalcinosis).
7. High-resolution computed tomography (HRCT) of chest.
8. Lung function tests (restrictive lung disease; also reduction of gas transfer).
9. Liver function tests (usually abnormal).
10. Bronchoscopy (shows cobble-stone appearance of mucosa).
11. Bronchoalveolar lavage (shows increased CD4:CD8 T-cell ratio. Increase neutrophil in pulmonary fibrosis).
12. Lung biopsy: Transbronchial or percutaneous (pneumothorax may develop), open biopsy may be required (by thoracotomy).
13. FNAC or biopsy from other involved site may be needed: Lymph node, skin nodule, liver, lacrimal gland, etc.
14. Others:
 - Angiotensin-converting enzyme in blood (increased level indicates active sarcoidosis; this test is not helpful for diagnosis).
 - ^{67}Gallium scanning of lung (abnormal diffuse uptake).
 - Kveim test: Intradermal injection of prepared sarcoid tissue in the forearm. In the positive case, formation of a nodule after 6 weeks. Biopsy is done from the nodule, which shows typical sarcoid lesion (**this test is not done now**).

Q: What are the **histopathological findings** in sarcoidosis?
A: Noncaseating granuloma consisting of epithelioid cells, macrophages and lymphocytes (mostly

T cells), and multinucleated giant cells (in TB, there is caseating epithelioid granuloma).

Q: What are the **radiological stages** of sarcoidosis?

A: 4 stages:

- Stage 1: BHL (usually symmetrical, may be paratracheal lymphadenopathy. May be associated with erythema nodosum, fever and polyarthralgia. Spontaneous resolution occurs in 1 year).
- Stage 2: BHL with parenchymal pulmonary infiltration (often diffuse, spontaneous resolution may occur).
- Stage 3: Diffuse pulmonary infiltrate without BHL (less likely to resolve spontaneously).
- Stage 4: Pulmonary fibrosis. The patient may complain of shortness of breath, cough. There is progressive ventilator failure, pulmonary hypertension and cor pulmonale. Spontaneous resolution is less likely to occur. (X-ray chest may show eggshell calcification.)

Q: Can there be **sarcoidosis and tuberculosis** together?

A: Yes. In sarcoidosis, there may also be tuberculosis.

Q: How to **treat** sarcoidosis?

A: As follows:

1. Acute with erythema nodosum: Bed rest with NSAID may be sufficient. If symptoms are severe, short-course steroid may be given. Spontaneous resolution occurs usually.
2. If the disease is not improved 6 months after the diagnosis, prednisolone should be given. Dose: Prednisolone 30 mg for 6 weeks, reduced to alternate day treatment with prednisolone 15 mg for 6 to 12 months.
3. Other treatment:
 - Avoid strong sunlight (may precipitate hypercalcaemia and renal impairment).
 - Topical steroid for uveitis.
 - Inhaled corticosteroid.
 - Chloroquine, hydroxychloroquine, low-dose thalidomide may be useful in cutaneous sarcoid.
 - In patient with severe disease: Methotrexate 10–20 mg weekly, or azathioprine 50–100 mg daily or TNF-α blocker (infliximab, etanercept).
 - Single lung transplantation may be done in selected case.

Indications of steroid:

- Severe symptoms such as persistent erythema nodosum, fever, arthritis or arthralgia.
- Parenchymal lung disease in any form.
- Vital organ involvement (eye, central nervous system, heart, kidney).
- Hypercalcaemia.

Prognosis: Mortality is 1–5%. Death is due to cardiac involvement, pulmonary fibrosis, and cor-pulmonale or renal damage.

Features suggestive of less favourable outlook:

- Age <40 years.
- Persistent symptoms >6 months.
- Involvement of more than three organs.
- Lupus pernio and stage 3 and 4 radiologically.
- Afro-Caribbean population.

CHAPTER 2

Cardiovascular System

"The heart moves of itself and does not stop unless forever"

– Leonardo da Vinci

Introduction

In any clinical examination, a case of cardiovascular system (CVS) is frequently selected. Also, it is an extremely common system tested in any oral examination. Very often, examiner asks, 'Examine the CVS'. However, many a times, examiner may ask to perform a particular part of CVS rather than the whole system and asks questions on that particular part. For example,

- Examine the CVS.
- Examine the precordium.
- Auscultate here... (examiner may point a particular part.)
- **Palpate** the pulse. What are your findings? (There may be no pulse or irregular, small- or high-volume pulse, bradycardia, tachycardia and pulse delay.)
- **Palpate** the pulse and **auscultate** the precordium. Describe your findings. [There may be low-volume, slow-raising pulse. On auscultation, ejection systolic murmur (ESM) may be present due to aortic stenosis (AS).]
- **Palpate** the precordium. What are your findings? (There may be tapping or shifting of the apex beat, heaving or thrusting in nature, thrill, palpable P2, left parasternal lift.)
- What are the diseases that can be diagnosed by palpation? (See later.)
- **Auscultate** the precordium. What are your findings? (Present systematically, starting from the heart sounds, murmur and any extra finding.)

To attain a good skill, see and examine more cases. Also, make a good practice to present systematically.

Remember, the examiner may interrupt at any part of your examination and ask, 'What is your finding? What is the more likely diagnosis for this finding only'?

Once you are asked to examine the CVS, the more likely underlying diseases are:

- Mitral stenosis [(MS) pure].
- Mitral regurgitation (MR).
- MS with pulmonary hypertension (PH).
- MS with MR (mixed mitral valve disease).
- AS or aortic regurgitation (AR)
- AS with AR (mixed aortic valve disease).
- Congenital heart disease [atrial septal defect (ASD), ventricular septal defect (VSD), patent ductus arteriosus (PDA) and dextrocardia].

Examination Routine

If the examiner asks to examine CVS, start examining systematically, including some **general examination** in relation to CVS.

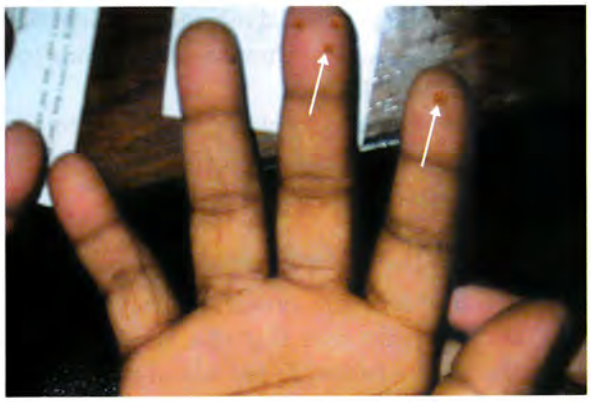
Proceed as follows:

Introduce yourself, 'I am Dr. ... May I examine your heart please'?

Position the patient at 45° with a backrest or pillows. With permission, remove the clothing to expose the chest and neck (be careful with a female patient).

1. **Look at the patient carefully:**
 - Dyspnoeic or orthopnoeic [left ventricular failure (LVF)], cachexia (in severe heart failure).
2. **Face:**
 - Malar flush (in MS).
 - Marfanoid face.
 - Corneal arcus and xanthelasma [related to atherosclerosis in ischaemic heart disease (IHD)], Argyll Robertson pupil (related to AR), mouth (high arch palate in Marfan syndrome).

3. **Anaemia.**
4. **Cyanosis** [tetralogy of Fallot (TOF) and Eisenmenger syndrome].
5. **Oedema** [leg and sacrum in congestive cardiac failure (CCF)].
6. **In hands:**
 - Clubbing.
 - Koilonychia.
 - Cyanosis.
 - Splinter haemorrhage.
 - Osler node (red, raised, palpable, tender nodule on the pulp of finger or toes; also in thenar or hypothenar area).
 - Janeway lesion (nontender, red, maculopapular lesion on palm or pulp of finger).
 - Xanthoma: Palmar or tendon (atherosclerosis in IHD).
 - Tobacco stain (smoker, **IHD**).



Osler node (in finger)



Osler node (in toe)

Now examine the pulse, jugular venous pressure (JVP), blood pressure (BP) and finally precordium.

Pulse

See the following points in radial pulse:

- Rate.
- Rhythm.
- Volume (make sure you lift the arm to see collapsing pulse).
- Character.
- Condition of the vessel wall.
- Radiofemoral delay and radioradial delay or inequality.

Compare other pulses simultaneously (carotid pulse should not be seen simultaneously). Volume and character of pulse are better seen in brachial and carotid artery. Collapsing pulse in AR and pulsus alternans in LVF are better seen in radial.

Neck Veins (JVP)

- The patient should be at 45°.
- Normal or engorged (internal jugular vein, lies medial to sternomastoid). If visible, see any prominent wave. See hepatojugular reflux by pressing firmly with palm over the middle of abdomen, which raises the upper limit of JVP. Next, measure the height from sternal angle. (It indicates mean right atrial pressure. Normally, it is at the level of sternal angle and invisible.)

Other signs in the neck:

- Tall, sinuous pulsation, oscillating up to the ear lobule (prominent V-wave) is found in tricuspid regurgitation (TR).
- Dancing carotid pulse (Corrigan sign in AR).
- Vigorous arterial pulsation in neck (coarctation of aorta).
- Other pulsation in neck (carotid aneurysm or subclavian artery aneurysm).

Blood Pressure

- Measure BP (normal or high). If needed, see in both arms. Also, in standing and lying (to see postural hypotension).
- Low systolic, normal diastolic and narrow pulse pressure (in AS).
- High systolic, low diastolic and wide pulse pressure (in AR).

Precordium

Inspection

- Deformity of chest (kyphosis, scoliosis, lordosis, pectus excavatum or carinatum).
- Visible cardiac impulse (visible apex beat).
- Other impulses (epigastric, suprasternal or any other impulse).

- Scar mark in the midline [valve replacement or coronary artery bypass grafting (CABG)], thoracotomy scar (valvotomy in MS).
- Pacemaker or cardioverter defibrillator box may be seen.

Palpation

1. **Apex beat:**
 - Site (Localise the intercostal space. Do not forget dextrocardia).
 - Distance from midline.
 - Nature (normal, tapping, heaving, thrusting and diffuse).
2. **Thrill:**
 - Site (apical or basal or other intercostal space).
 - Nature (systolic or diastolic): Feel carotid pulse at the same time. If coincides with carotid pulse, it is systolic and if it does not coincide (comes after or before), it is diastolic.

 N.B. See apical and basal thrill. Apical thrill is best seen by turning the patient to left lateral position with breathing held after expiration; apex comes closer to the chest wall. Basal thrill is best seen by palm with the patient sitting and bending forward, breathing held after expiration (base of heart comes closer to the chest wall).

3. **Left parasternal heave or lift:** Place the flat of right palm in left parasternal area and feel by giving gentle sustained pressure [presence of left parasternal heave indicates right ventricular hypertrophy (RVH)].
4. **Palpable P2** (if present, indicates PH).
5. **Epigastric pulsation.**

Percussion

Usually not done; may be helpful to diagnose pericardial effusion (area of cardiac dullness is increased) and emphysema (cardiac dullness is obliterated).

Auscultation

1. See first and second heart sounds in all areas. At the same time, palpate right carotid pulse simultaneously with thumb. **(Yes! Examiner notices.) First heart sound** coincides with carotid pulse, the **second sound** does not (comes after).
2. Murmur:
 - Site (apical, parasternal, aortic or pulmonary area).
 - Nature: Systolic (pansystolic or ejection systolic), diastolic (mid-diastolic or early-diastolic) by feeling carotid pulse at the same time (systolic coincides with carotid pulse, and diastolic does not coincide).
 - Radiation (PSM to left axilla and ESM to neck).
 - Relation with respiration (right-sided murmur increases on inspiration and left-sided murmur increases on expiration).
 - Grading of murmur (2/6 or 4/6).
3. Added sounds (pericardial rub and opening snap).
4. Auscultate the back of chest for crepitations (pulmonary oedema).
5. Ask for permission to palpate the liver (enlarged tender liver in CCF, pulsatile liver in TR) and spleen (splenomegaly in SBE).

N.B. Remember the following points:

- If mid-diastolic murmur (MDM) is present at apex, make sure that you have listened by turning the patient in left lateral position with the bell of stethoscope with breathing held after expiration. **(Yes! Examiner notices.)**
- If early-diastolic murmur (EDM) is present, make sure that you have listened with the patient sitting and bending forward with breathing held after expiration.
- If presystolic murmur (PSM) is present, put your stethoscope in axilla to see radiation.
- If ESM is present, put your stethoscope on right carotid to see radiation.

Important Discussions in Relation to CVS

Pulse

A. Rate

- Tachycardia: When the pulse rate is >100/min.
- Bradycardia: When the pulse rate is <60/min.

Causes of **tachycardia:**

- Sinus tachycardia due to any cause (see below).
- Supraventricular tachycardia.
- Atrial fibrillation (AF) and atrial flutter.
- Ventricular tachycardia.

Causes of **sinus tachycardia:**

1. Physiological (anxiety, emotion, exercise and pregnancy).
2. Pathological: Hyperdynamic circulation [fever, anaemia, thyrotoxicosis, arteriovenous (AV) fistula and beriberi].

- CCF.
- Myocarditis.
- Chronic constrictive pericarditis.
- Shock (except vasovagal attack).
- Acute anterior myocardial infarction (MI; except inferior MI).
- Sick sinus syndrome.
- Pulmonary embolism.
- Drugs (salbutamol, atropine and other sympathomimetics).

Causes of **bradycardia:**

1. Sinus bradycardia due to any cause (see below).
2. Second-degree heart block.
3. Complete heart block.
4. Nodal rhythm.

Causes of **sinus bradycardia**

1. Physiological (due to increased vagal tone): Athlete, during sleep.
2. Pathological:
 - Acute inferior MI.
 - Myxoedema (due to reduction of sympathetic activity).
 - Hypothermia. Raised intracranial tension (due to inhibitory effect on sympathetic outflow). Obstructive jaundice (due to deposition of bilirubin in conducting system).
 - Drugs (digoxin, β-blockers, amiodarone and verapamil).

B. Rhythm

It is the interval between successive pulses. It may be regular or irregular. Irregular rhythm may be irregularly irregular or regularly irregular.

Causes of **irregular pulse:**

1. **Regularly irregular (follows a definite pattern of regular rhythm followed by irregular rhythm). It occurs in:**
 - Sinus arrhythmia (pulse rate increases on each inspiration, decreases on each expiration). It is abolished by exercise.
 - Occasional ectopics. Second-degree heart block (Mobitz type I, Wenckebach type).
2. **Irregularly irregular means irregular in rhythm and volume. Its causes are:**
 - Atrial fibrillation.
 - Multiple ectopics.
 - Atrial flutter with variable block.
 - Paroxysmal atrial tachycardia with variable block.

Q: How to **differentiate** between AF and multiple ectopics in bedside?

A: By physical exercise. With exercise, ectopics will disappear, but AF will be more prominent [needs electrocardiography (ECG) for confirmation].

C. Volume of Pulse

Causes of **high-volume pulse**

- AR.
- Hyperdynamic circulation due to any cause.
- PDA.
- Hypertension.

Causes of **low-volume pulse**

- Shock.
- AS.
- MS.
- Chronic constrictive pericarditis.
- Pericardial effusion.
- PH

D. Character of Pulse

1. Anacrotic pulse is a slow-raising, small-volume pulse (notch on upstroke). It is caused due to AS.
2. Plateau pulse is of small volume with slow upstroke. It is caused due to AS.
3. Bisferiens pulse is the double peak of pulse, which is felt better in carotid (due to combination of slow raising and collapsing). Caused due to combined AS and AR.
4. Water hammer pulse is typically found in AR (see page 85).
5. Pulsus alternans is an alternate strong and weak beat (suggestive of LVF).
6. Jerky pulse is seen in carotid artery. It is caused due to hypertrophic cardiomyopathy (HCM).
7. Pulsus paradoxus: When volume of pulse reduces on inspiration and increases on expiration, it is called pulsus paradoxus (also systolic BP falls during inspiration, normally <10 mmHg). It is the exaggeration of normal phenomenon (normally present in children). It is better detected by sphygmomanometer. Abnormal, if >10 mmHg.

 Causes of pulsus paradoxus:

 - Pericardial effusion (especially, cardiac tamponade).
 - Chronic constrictive pericarditis.
 - Acute severe asthma and chronic obstructive pulmonary disease (COPD).
 - Massive pulmonary embolism.

Mechanism of pulsus paradoxus: During inspiration, intrathoracic pressure falls, blood pools in pulmonary vessels and hence left heart filling is reduced with reduction of cardiac output. Therefore, the pulse volume is low, which is reverse on expiration.

8. Collapsing pulse: There is a rapid upstroke and descent of pulse, seen by raising the arm above the head. Causes are:
 - AR (the commonest cause).
 - Hyperdynamic circulation due to any cause (see above).
 - PDA.
 - Rupture of sinus of Valsalva. Large arteriovenous communication.

Q: What is the **difference** between high-volume pulse and collapsing pulse?

A: Collapsing pulse is always a high-volume pulse, but all the high-volume pulses are not necessarily collapsing.

JVP

(See internal jugular vein, which lies along the medial border of sternomastoid. External jugular vein is not examined as it is tortuous and subject to compression.) Normally, it is 2 cm. If >3 cm, right heart filling pressure is raised. It is a sign of right heart failure or volume overload.

Causes of raised JVP:

- CCF (right heart failure).
- Pericardial effusion.
- Chronic constrictive pericarditis.
- Pulmonary embolism.
- Tricuspid regurgitation (TR) and tricuspid stenosis (TS).
- Pulmonary regurgitation and pulmonary stenosis (PS).
- Superior vena caval (SVC) obstruction (nonpulsatile).
- Others: Occasionally may occur in pregnancy, exercise, anxiety and anaemia.

Causes of prominent **'a' wave in JVP** (comes just before carotid pulse):

- PH.
- Pulmonary embolism.
- TR and TS.
- PS.

Q: What are the **differences** between venous pulse or arterial pulse in neck?

A: As follows:

	Venous	Arterial
1.	It is wavy (two peaks with cardiac cycle)	Not wavy
2.	It has an upper limit	No definite upper limit
3.	Upper limit falls with inspiration	Not so
4.	Varies with posture	Independent of posture
5.	It is better seen than palpation	It is better felt than seen
6.	Upper limit is increased by pressing the abdomen (hepatojugular reflux)	Not so
7.	Just felt or lightly felt	Thrusting
8.	It is obliterated by light pressure at the root of the neck and then filled from above	Cannot be obliterated

Causes of **cannon wave** (giant 'a' wave): Occurs when atria contracts against closed tricuspid valve

- Complete heart block ('a' wave is intermittent).
- Junctional rhythm (regular cannon wave).
- Ventricular tachycardia ('a' wave is intermittent).

Giant 'v' wave is tall, sinuous, oscillating up to ear lobule. It is caused due to TR.

Causes of giant **X descent** are chronic constrictive pericarditis and cardiac tamponade.

Cause of slow **Y descent** is TS.

Kussmaul sign: It means raised JVP during inspiration due to reduction of right ventricular output. It is best seen with the patient at 90° with normal breathing (normally, JVP falls during inspiration). Its causes are:

- Pericardial effusion (usually, cardiac tamponade).
- Chronic constrictive pericarditis.
- Right ventricular infarction.

Corrigan sign: Dancing carotid pulse is called Corrigan sign. It is caused due to AR.

Carotid pulse is prominent and forceful; it may be seen in:

- Coarctation of aorta.
- Aneurysm of aorta.
- Carotid artery aneurysm.
- Subclavian artery aneurysm.
- Others: Hyperdynamic circulation, AR and anxiety.

Precordium

Deformity of chest (kyphosis, scoliosis, pectus excavatum and pectus carinatum) may be associated with Marfan syndrome, cor pulmonale.

Apex Beat

It is the lowermost and outermost, definitely palpable cardiac impulse. It is normally 9 cm from midline or 1 cm internal to the midclavicular line in left fifth intercostal space. Apex beat may be heaving, thrusting or tapping in nature.

- Heaving: Forceful, sustained, lifting the examining finger (pressure overload). It indicates left ventricular hypertrophy (LVH) (due to hypertension and AS).
- Thrusting: Forceful, less sustained, lifting the examining finger (volume overload). It indicates left ventricular dilatation (as in MR and AR). Also called hyperkinetic or dyskinetic apex. Felt over larger area of precordium.
- Tapping apex: Neither sustained nor forceful, not lifting the finger. It is the palpable first heart sound. Found in MS (rarely TS).

Causes of double apex beat

- Ventricular aneurysm.
- HCM.

Causes of impalpable apex beat

- Thick chest wall (obesity).
- If the apex is behind the rib.
- Emphysema.
- Pericardial effusion.
- Dextrocardia (apex is on the right side).

Causes of diffuse apex beat

- Anterior MI (better seen).
- Occasionally, in left ventricular aneurysm.

Left parasternal **heave** or **lift** indicates RVH (in PH, cor pulmonale, PS and pulmonary regurgitation, and TR).

Causes of epigastric pulsation:

- Normally palpable (lean and thin person).
- RVH.
- Aneurysm of abdominal aorta (expansile pulsation).
- Mass overlying aorta (carcinoma of stomach).
- Pulsatile liver (in TR).

Suprasternal pulse: Usually arterial (due to aneurysm of aorta and atherosclerosis).
Pulsation around scapula: Due to coarctation of aorta (due to anastomotic vessels).

Heart Sounds

1. First heart sound:
 - Loud in MS, TS (occasionally in anxiety, exercise).
 - Soft or absent in MR, myocarditis and cardiomyopathy.
2. Second heart sound: Splitting is better heard in pulmonary area, in inspiration due to prolonged right ventricular systole.

 Causes of **wide splitting** of second sound:
 - PS.
 - Right bundle branch block (RBBB).
 - Atrial septal defect (ASD).
 - Cause of **wide and fixed splitting** of second sound: ASD.

 Causes of **reverse splitting** of second sound (A2 is delayed):
 - Left bundle branch block (LBBB).
 - AS.
 - Hypertension.

 Causes of **loud** second sound:
 - Systemic hypertension.
 - PH.

 Causes of **soft** second sound:
 - Calcified or severe AS.
 - Severe PS.
 - AR.
3. Third heart sound: Low-pitched, distant sound due to ventricular filling, and comes after second sound. It is better heard at the apex with bell of stethoscope. Its causes are:
 - Physiological: In young, in athlete, during pregnancy and in fever.
 - Pathological: LVF, MR, anaemia, cardiomyopathy, AR, chronic constrictive pericarditis. (This third sound is called pericardial knock.)
4. Fourth heart sound: Low-pitched sound due to atrial contraction, precedes first heart sound, better heard at the apex. Causes are (ventricular failure and ventricular hypertrophy):
 - Due to left heart, hypertension, AS, IHD and HCM.
 - Due to right heart, PS and PH.

Triple Rhythm

When in addition to first and second heart sounds, there is another sound that is either third or fourth, it is called triple rhythm.

Gallop Rhythm

When triple rhythm is associated with tachycardia (>100), it is called gallop rhythm.

It is called 'gallop' as the cadence of sound resembles a galloping horse.

Gallop rhythm is of three types:

- Protodiastolic: Extra sound (third heart sound), in early- or mid-diastole.
- Presystolic: Extra sound (fourth heart sound) in late diastole.
- Summation: When third and fourth heart sounds coalesce, it is called summation gallop, usually with heart rate >120.

Presence of gallop rhythm indicates cardiac failure (LVF).

Murmur

It is a blowing sound produced by turbulent blood flow in the heart. The murmur is produced by either normal volume of blood passing through abnormal valve or increased volume of blood passing through a normal valve or congenital defect. Murmur may be:

- Systolic.
- Diastolic.
- Continuous.

Systolic murmur

Pansystolic murmur (PSM). Its causes are:

- MR.
- TR.
- VSD.
- Aortopulmonary shunt.

Ejection systolic murmur (ESM; harsh and high pitched). Its causes are:

- AS.
- PS.
- HCM.
- ASD (due to increased flow through pulmonary valve).
- Other causes are due to increased flow (in pregnancy, fit athlete).

Late systolic; it is found in mitral valve prolapse and also in papillary muscle dysfunction.

Diastolic murmur

EDM (soft, high pitched, blowing). Its causes are:

- AR.
- Pulmonary regurgitation (Graham Steell murmur in left second, third, and fourth space).

MDM. Its causes are:

- MS.
- TS.
- Left atrial myxoma.
- Austin Flint murmur in AR.
- Carey Coombs murmur (due to mitral valvulitis in acute rheumatic fever, RF).
- ASD (due to increased flow through tricuspid valve).

Continuous murmur

Present in both systole and diastole. Its causes are:

- PDA.
- AV fistula (coronary, pulmonary or systemic).
- Aortopulmonary fistula (may be congenital or Blalock–Taussig shunt).
- Venous hum.
- Rupture of sinus of Valsalva to right ventricle or atrium.

Innocent murmur

Benign, usually soft systolic, present in upper sternal edge (commonly pulmonary area), found in some normal people without heart problem. Not associated with thrill and grade of murmur is up to 2/6. (Systolic murmur may be present also in anaemia, thyrotoxicosis and pregnancy.)

Grading of murmur

- Grade 1/6: Very soft murmur, just audible.
- Grade 2/6: Soft.
- Grade 3/6: Moderately loud.
- Grade 4/6: Loud (thrill present).
- Grade 5/6: Very loud (thrill present).
- Grade 6/6: Very much loud, heard without placing the stethoscope over the chest (thrill present).

Thrill is present in grades 4–6.

Pericardial Rub

- Superficial, harsh, scratching, creaking, grating and leathery sound.
- Present in both systole and diastole.
- Louder with the patient sitting, breathing out and bending forward.
- Augmented by pressing the stethoscope. It is present with breath holding.
- Heard in any area of precordium, better heard in **bare area of heart** (part of heart not covered by the lung, this part is close to chest wall, in left lower sternum).
- Presence of pericardial rub indicates pericarditis due to any cause [such as acute MI, viral infection, uraemia and tuberculosis (TB)].

Opening Snap

Short, sharp, high-pitched sound heard immediately after second heart sound (during diastole), produced by sudden opening of mitral valve due to raised left atrial pressure (in MS).

Presence of opening snap indicates that the valve cusps are still mobile. It is absent, if the valve is calcified. Opening snap is better heard in left lower sternal edge.

Venous Hum

It is a continuous murmur due to kinking and partial obstruction of one of the large veins in the neck. It is found in the neck above the clavicle and upper part of chest, more on the right side of sternum.

The hum can be obliterated by pressure on the neck, or lying down or altering the position of neck (as there is reduction of venous obstruction).

It is accentuated by sitting with head extended and turned to the side opposite to that auscultated.

Venous hum has no clinical significance, commonly present in children and should not be confused with any pathology.

Other Sounds

- Tumour plop is found in myxoma.
- Metallic sounds are found in prosthetic metallic valve.

Mitral Stenosis

Presentation of Case No. 1

- Pulse: 84/min, low volume, and normal in rhythm and character.
- JVP: Normal ('a' wave is prominent, if PH is present, and 'a' wave is absent in AF).
- BP: 100/60 mmHg.

On inspection:

- Visible cardiac impulse in mitral area.

On palpation:

- Apex beat: In left fifth intercostal space, ... cm from midline and tapping in nature.
- Thrill: Present in apical area, diastolic in nature (also see in left lateral position with breath held after expiration).

On auscultation:

- First heart sound: Loud in all areas (occasionally only in mitral area and normal in other areas).
- Second heart sound: Normal in all areas [if pulmonary hypertension (PH), P2 is loud].
- There is an MDM in mitral area, which is low pitched–localised–rough–rumbling (LLRR), best heard with bell of stethoscope in left lateral position, breathing held after expiration, with presystolic accentuation.
- Opening snap (tell, if present).

My diagnosis is **MS.**

N.B. If the murmur is not audible, ask permission that the patient should perform physical exercise. This will increase the heart rate, increase the flow across the mitral valve and murmur will be prominent. However, **exercise should be avoided** in very ill patient.

Presentation of Case No. 2

Present as above **plus.**

- Palpable P2.
- Left parasternal heave.
- Loud P2 on auscultation.

My diagnosis is **MS with** PH.

Q: What are the signs of pulmonary hypertension?

A: Signs of pulmonary hypertension are:

- Low-volume pulse.
- Prominent 'a' wave in JVP.
- Palpable P2.
- Left parasternal heave (indicates RVH).
- Epigastric pulsation (indicates RVH).
- Loud P2 on auscultation.
- EDM (Graham Steell murmur due to pulmonary regurgitation).

Presentation of Case No. 3

- Pulse: 110/min, irregularly irregular.
- Pulsus deficit is present.
- No 'a' wave in JVP.
- No presystolic accentuation.
- Other findings are same as in MS.

My diagnosis is **MS with atrial fibrillation.**



Mitral facies

Q: What do you **think** is the cause in this case?
A: Chronic rheumatic heart disease.

Q: If this patient is unconscious, what is the likely cause?
A: Cerebral embolism (usually with right-sided hemiplegia because of lesion in the internal capsule due to involvement of the lenticulostriate branch of left-middle cerebral artery).

Q: What are the findings if the patient develops CCF?
A: Three cardinal signs of CCF are:
- Engorged and pulsatile neck veins.
- Enlarged tender liver.
- Dependant oedema.

Q: Which **disease confuses** with MS? (Or, what are the differential diagnoses of MS?).
A: As follows:
- Left atrial myxoma (murmur will change with posture, see below).
- Ball-valve thrombus in left atrium.
- TS.

Q: Why **not** this is TS?
A: In TS, MDM is prominent in left lower parasternal edge, which increases during inspiration. Also, there may be other features such as raised JVP and signs of right heart failure.

Q: Why **not** this is left atrial myxoma?
A: In left atrial myxoma, physical signs and murmur change with posture. Also, there may be history of fever, weight loss, myalgia, arthralgia, skin rash, Raynaud phenomena (which are absent in this case). To be confirmed, 2-D echocardiography should be done.

Q: What are the **causes** of MS?
A: As follows:
1. Chronic rheumatic heart disease (the commonest cause). In 50% cases, there may be history of RF or rheumatic chorea.
2. Other causes are (very rare, do not mention unless asked):
 - Congenital.
 - Calcification of valve (usually in elderly).
 - Carcinoid syndrome.

(MS is more common in females. F:M = 2:1).

Q: What is **Lutembacher syndrome**?
A: Combination of ASD with acquired rheumatic MS (occurs in 4% cases of ASD).

Q: Why apex beat is **tapping**?
A: It is due to accentuated first heart sound.

Q: When and why the **presystolic accentuation** is present?
A: It is due to atrial systole, present in sinus rhythm. It occurs due to increased flow across the stenosed valve from left atrium to left ventricle causing loudness of murmur. Presystolic accentuation is absent in AF.

Q: What is **mitral facies** or **malar flush**?
A: It is the rosy colouration of cheeks, may be bluish tinge, due to arteriovenous anastomosis and vascular stasis on the cheeks. It is not pathognomonic and may be present in normal person, and persons with hypothyroidism, polycythaemia and PH.

Q: What are the **signs of severe MS**?
A: Normal area of mitral valve is 4–6 cm^2. Severe, if <1 cm^2.

Signs of severe MS
- Pulse: Low volume.
- First heart sound: Soft.
- MDM: Prolonged.
- Opening snap: Closer to second heart sound.
- Signs of PH.
- Later, opening snap disappears and MDM quiet (due to low cardiac output).

Q: What are the **mechanisms** of pulmonary hypertension in MS?

A: As follows:

- Passive backward transmission of raised left atrial pressure.
- Reflex pulmonary artery vasoconstriction.
- Organic obliterative change in pulmonary vascular bed.

Q: What are the **complications of MS?**

A: As follows:

- Atrial fibrillation.
- Pulmonary oedema.
- PH leading to CCF.
- Pulmonary infarction.
- Systemic embolism: Commonly cerebral (cerebral infarction with hemiplegia), also in mesenteric, renal and peripheral.
- Haemoptysis.
- Ortner syndrome (enlarged left atrium exerts pressure on left recurrent laryngeal nerve and causes hoarseness of voice).
- Dysphagia due to enlarged left atrium.
- Interstitial lung disease due to prolonged pulmonary oedema.
- Chest pain in 10% cases (due to PH).
- Infective endocarditis (very rare).

Q: If the patient suddenly becomes **unconscious**, what is the likely cause?

A: Cerebrovascular disease [(CVD) cerebral infarction], usually with right sided hemiplegia. Usually CVD occurs when there is associated atrial fibrillation (AF).

Q: What may be the **cause of CVD** in this case?

A: Cerebral embolism (involving lenticulostriate branch of the left middle cerebral artery causing infarction of the internal capsule).

Q: Why **syncope** may occur in MS?

A: Due to reduction of cardiac output. Also may be due to atrial fibrillation with fast ventricular rate, PH, pulmonary embolism, ball valve thrombus, cerebral embolism.

Q: What is the cause of **haemoptysis** in MS?

A: Rupture of pulmonary or bronchial veins associated with PH (pulmonary apoplexy). Also, haemoptysis may be due to pulmonary infarction.

Q: What **investigations** do you suggest?

A: As follows:

- Chest X-ray.
- ECG: P is bifid (P-mitrale), RVH and RAH.
- 2-D echocardiogram and colour Doppler.
- Cardiac catheterisation in some cases.

Q: What are the **findings** in chest X-ray in MS?

A: Chest X-ray shows:

- Upper lobe veins are dilated (early feature): Upper lobe diversion (normally, ratio between upper and lower lobe veins is 1:3, which is altered to 1:1).
- Straightening of left border of heart, fullness of pulmonary conus and filling of pulmonary bay (due to enlarged left atrium).
- Kerley B-lines (horizontal septal lines in costophrenic angle indicates PH).
- Double shadow in right border of heart (due to enlarged left atrium).
- Widening of carina.
- Left bronchus is horizontal (due to enlarged left atrium).
- Pulmonary oedema.
- Mottling or reticulonodular shadow due to pulmonary haemosiderosis.
- Calcified shadow of mitral valve.

Q: What are the **echocardiogram** findings in MS?

A: As follows:

- Thick mitral valve leaflet (with restricted opening), diastolic doming of anterior mitral leaflet and restricted movement of posterior mitral leaflet.
- Reduction of valvular area (narrow): Button-like or funnel shaped.
- Calcification of valves (increased echogenicity).
- Shortening of chordae tendineae.
- Enlarged left atrium.
- Characteristic 'M'-shape of movement of anterior leaflet normally seen in diastole is lost and the diastolic slope (EF) is reduced.
- Thrombus may be seen.

Q: How to **treat** MS medically?

A: As follows:

- Restrictive activity.
- Anticoagulant to reduce the risk of embolism.
- If atrial fibrillation: Digoxin, β-blocker, rate-limiting calcium antagonist (e.g. verapamil, diltiazem).
- If there is CCF: Diuretics, digoxin.
- Infective endocarditis is very unusual in MS. So, routine prophylaxis with antibiotic is not recommended.

Q: What are the indications of anticoagulant (warfarin) in MS?

A: As follows:

- Systemic and pulmonary embolism.
- Atrial fibrillation.

- Left atrial thrombus.
- Left ventricular systolic dysfunction.

Q: What are the **indications of surgery** in MS?

A: As follows:

- Symptomatic moderate or severe MS when balloon valvuloplasty is unavailable.
- Moderate or severe MS with moderate or severe MR.
- Recurrent thromboembolism.
- Episodes of pulmonary oedema without precipitating cause.
- Associated atrial fibrillation, which does not respond to medical therapy.
- PH or recurrent haemoptysis.
- Occasionally in pregnancy, with pulmonary oedema (surgery may be done in second trimester as blood volume increases significantly with increased pulmonary pressure).

Q: What **surgery** is usually done?

A: As follows:

- Valvotomy [closed mitral commissurotomy (CMC), open mitral commissurotomy (OMC)].
- Valvuloplasty (percutaneous balloon mitral valvuloplasty): Treatment of choice.
- Valve replacement.

Q: What are the **criteria for valvuloplasty**?

A: As follows:

- Significant symptoms.
- Pure MS.
- No or trivial MR.
- Valve: Mobile, no calcification.
- Left atrium: No thrombus.

Q: What are the **indications of valve replacement**?

A: As follows:

- Associated MR.
- If the valve is calcified and rigid.
- Thrombus in left atrium despite anticoagulation.

Q: What are the **complications** of surgery?

A: As follows:

- MR.
- Thromboembolism.
- Restenosis.

Q: What is the **contraindication** of surgery in MS?

A: Active rheumatic carditis.

Q: How to **treat MS in pregnancy**?

A: As follows:

- Bed rest.
- Correction of anaemia.
- Correction of nutrition.
- If severe, symptomatic and tight MS: Mitral valvotomy may be done (usually in middle trimester).
- All patients should go into full term and Caesarean section should be done.
- Advice the patient to restrict number of pregnancy (1–2).

N.B. Symptoms of MS are usually more marked in second trimester, which is due to increase in blood volume that increases pulmonary pressure. The symptoms improve in third trimester due to decrease in blood volume.

Q: What is **myxoma** of the heart? What are the **features**? How to **investigate** and **treat**?

A: It is the common primary tumour of heart, usually benign, may be pedunculated, polypoid, gelatinous, attached by a pedicle to the atrial septum. It may be sporadic and familial. It occurs at any age (third–sixth decade of life) and any sex (more in female).

Sites of origin:

- Left atrium (75%), near the fossa ovalis or its margin.
- Right atrium, rarely from ventricles.

Clinical features: There are three groups of manifestations.

1. Obstructive features: Such as MS, signs vary with posture. Occasionally, there is a low-pitched sound called *tumour plop*. There may be syncope or vertigo.
2. Embolic features: Either systemic or pulmonary embolism.
3. Constitutional features: Such as fever, malaise, weakness, loss of weight, myalgia, arthralgia, clubbing, skin rash, Raynaud phenomenon.

Investigations:

- CBC: Anaemia, leucocytosis, polycythaemia, high ESR, thrombocytopaenia or thrombocytosis
- Hypergammaglobulinaemia.
- Chest X-ray (may be similar to MS).
- Echocardiogram: 2-D or transoesophageal.
- CT scan or MRI may be done.

Treatment: Surgical excision. Recurrence may occur.

N.B. Other tumours of the heart are rhabdomyoma and sarcoma. All are rare.

Mitral Regurgitation

Usual instructions are:

- Examine the precordium. Or, palpate and auscultate the precordium.

Presentation of a Case

- Pulse: 80/min, normal volume, rhythm and character.
- JVP: Normal.
- BP: 120/70 mmHg.

On inspection:

- Visible cardiac impulse in mitral area.

On palpation:

- Apex beat in left ... intercostal space, ... cm from midline, diffuse, thrusting in character.
- Systolic thrill in left ... intercostal space.

On auscultation:

- First heart sound: Soft in mitral area, normal in other areas.
- Second heart sound: Normal in all the areas (third heart sound: may be present).
- There is a PSM in mitral area, which radiates to the left axilla (PSM is reduced on inspiration and more in expiration).

My diagnosis is **MR**.

Q: Can there be **any** MDM in MR?

A: Yes, it may be present due to increased flow of blood through mitral valve (or if associated with MS).

Q: What are the causes of pansystolic murmur?

A: As follows:

- MR.
- TR.
- VSD.

Q: What are your **differential diagnoses**?

A: As follows:

- TR.
- VSD.

Q: Why not this is **tricuspid regurgitation** (TR)?

A: Because in TR:

- PSM is in left lower parasternal area.
- No radiation to axilla.
- Murmur is prominent on inspiration and less on expiration.
- Raised JVP with prominent V-wave.
- Liver is enlarged, tender and pulsatile.

Q: Why **not** VSD?

A: Because in VSD:

- Systolic thrill in left parasternal area (fourth or fifth space).
- PSM in left parasternal area (fourth or fifth space). No radiation of murmur to axilla.

Q: What are the **causes** of MR?

A: As follows:

- Chronic rheumatic heart disease (rheumatic MR is more common in male).
- Mitral valve prolapse.
- Papillary muscle dysfunction (due to acute inferior myocardial infarction).
- Rupture of chordae tendineae (due to infarction, subacute bacterial endocarditis, trauma or spontaneous).
- Infective endocarditis.
- Valvotomy or valvuloplasty.
- Connective tissue diseases (RA and SLE).
- Ankylosing spondylitis.
- Cardiomyopathy.
- Secondary to LV dilatation (hypertension, aortic valve disease).
- Associated with Marfan syndrome, pseudoxanthoma elasticum and Ehlers–Danlos syndrome.

Q: What are the **causes** of acute MR?

A: As follows:

- Trauma or surgery (valvotomy).
- SBE (due to perforation of mitral valve leaflet or chordae).
- Acute MI (due to rupture of papillary muscle).
- Acute rheumatic fever (RF) (due to mitral valvulitis).
- Spontaneous rupture of chorda tendineae or myxomatous degeneration of valve.

Q: Where does the murmur **radiate** following rupture of chorda tendineae?

A: As follows:

- Rupture of anterior leaflet of chorda tendineae, murmur radiates to axilla and back.
- Rupture of posterior leaflet of chorda tendineae, murmur radiates to cardiac base and carotid arteries.

Q: What are the **complications** of MR?

A: As follows:

- Acute LVF.
- Infective endocarditis.
- Systemic embolism (less than MS).
- Atrial fibrillation.
- CCF.

Q: What **investigations** do you suggest?

A: As follows:

- Chest X-ray (heart size is enlarged in transverse diameter TD).
- ECG (LVH).
- 2-D echocardiogram and colour Doppler.
- Cardiac catheterisation, in some cases.

Q: What are the **signs** of severe MR?

A: As follows:

- Enlarged left ventricle (apex is shifted and thrusting).
- Presence of third heart sound.
- Appearance of short MDM (due to rapid filling of left ventricle).

Q: How to **treat** MR?

A: As follows:

1. Mild to moderate case, give symptomatic treatment:
 - Diuretics.
 - Vasodilators (ACE inhibitor may be used).
 - Follow-up every 6 months by echocardiogram.
2. Severe or progressive MR or if the ejection fraction falls to 55% and left ventricular dilatation is > 60 mm, then valve replacement is needed. If papillary muscle rupture or chorda tendineae rupture in SBE, early valve replacement is suggested.

Mitral Valve Prolapse (Barlow Syndrome or Floppy Mitral Valve)

Usual instructions are:

- Examine the precordium. Or, palpate and auscultate the precordium.

Presentation of a Case

Present the case as described for MR **plus** the following:

- Mid-systolic click.
- Late-systolic murmur (loudest at the left sternal edge).

Cardinal signs are **(hallmark)** mid-systolic click and late systolic murmur (loudest at the left sternal edge).

Q: What is **mitral valve prolapse?**

A: It is also called Barlow syndrome or floppy mitral valve. In this condition, a mitral valve leaflet (most commonly the posterior leaflet) prolapses into the left atrium during ventricular systole. It is one of the commonest causes of MR. It may be congenital anomaly or due to degenerative myxomatous changes.

Q: How the patient **presents?**

A: Mitral valve prolapse is more common in thin, young women, may be familial.

- Asymptomatic. It may be present in healthy women in up to 10% cases. Symptoms increases with aging.
- The commonest symptom is atypical chest pain, usually in left submammary region and stabbing in quality (due to abnormal ventricular contraction or atrial or ventricular dysrhythmia).
- Rarely, it may be confused with anginal pain.
- There may be palpitation, dyspnoea, fatigue, benign arrhythmia or rarely fatal ventricular arrhythmia. Embolic stroke and TIA are rare complications.

Q: What are the **complications** and **associations** of mitral valve prolapse?

A: Complications are:

- May cause MR.
- Infective endocarditis (rare).
- Embolic stroke and TIA are rare complications.

Associations:

- SLE.
- Marfan syndrome.
- Ehlers–Danlos syndrome.
- Osteogenesis imperfecta.
- Pseudoxanthoma elasticum.
- HCM or congestive cardiomyopathy.
- Muscular dystrophy.
- ASD (20%).
- Anorexia nervosa.

Investigations:

- ECG: Nonspecific ST- or T-wave change.
- Echocardiography.

Treatment:

- Asymptomatic patient only needs reassurance, periodic echocardiography may be done.
- Atypical chest pain and palpitation are treated with β-blockers. Other antiarrhythmic drugs may be needed.
- If there is significant MR or AF, anticoagulation is indicated to prevent thromboembolism (aspirin may be given).
- If MR is severe, mitral valve repair or replacement should be done.

N.B. Prophylaxis for infective endocarditis in most cases is not recommended. Overall prognosis is good.

Mitral Stenosis with Mitral Regurgitation (Mixed Mitral Valve Disease)

Usual instructions are:

- Examine the precordium. Or, palpate and auscultate the precordium.

(In mixed valvular lesion, candidate may be asked about **dominant** lesion.)

Presentation of Case No. 1: Predominant MS

- Pulse: 88/min, low in volume, normal rhythm and character.
- JVP: Normal.
- BP: 115/60 mmHg.

On inspection:

- Visible cardiac impulse in mitral area.

On palpation:

- Apex beat: In left ... intercostal space, ... cm from midline, and tapping in nature.
- Thrill: Present in apical area, both systolic and diastolic.

On auscultation:

- First heart sound, louder in all areas (may be in mitral area, normal in other areas).
- Second heart sound, normal in all areas.
- There is an MDM in mitral area and also a PSM in mitral area, which radiates to left axilla.
- There is also opening snap (mention, if any).

My diagnosis is **MS with** MR.

Q: What is the **predominant lesion** and why?
A: Predominant lesion is MS, because:

- Pulse: Low volume.
- Apex beat: Tapping in nature and not shifted.
- First heart sound: Loud.

Q: What are the findings, if **MR is predominant**?
A: If MR is predominant:

- Pulse: Normal volume.
- Apex beat: Shifted and thrusting in nature.
- First heart sound: Soft or absent.
- Third heart sound: May be present.

Q: What is the **cause** of mixed MS and MR?
A: Chronic rheumatic heart disease.

Presentation of Case No. 2: Predominant MR

Present as in Case no. 1, except the following:

- Pulse: Normal in volume.
- Apex beat: Shifted and thrusting in nature.
- First heart sound: Soft.
- There is also third heart sound (mention if any).

My diagnosis is MR **with MS.**

Q: What is the **predominant** lesion and why?
A: Predominant lesion is MR, for reasons see above.

Q: What happens, if MS is predominant?
A: See above.

Q: What **investigations** do you suggest?
A: As follows:

- Chest X-ray, PA view.
- ECG.
- 2-D echocardiogram and colour Doppler.
- Cardiac catheterisation, in some cases.

N.B. Occasionally, difficulty arises, when, for example, the patient has loud first heart sound and apex beat is also displaced. In such cases, you should say that, 'it is difficult to be sure clinically about the dominant lesion. Echocardiogram is necessary'.

Q: In which lesion—MR or MS, **endocarditis is common**?
A: Endocarditis is common in MR.

Q: How to **treat** mixed MS and MR?
A: As follows:

- Mild and asymptomatic: Follow-up is needed.
- In severe and symptomatic case: Valve replacement is required.

Aortic Stenosis

Usual instructions are:

- Examine the precordium. Or, palpate and auscultate the precordium.

Presentation of a Case

- Pulse: 76/min, low volume and slow raising, normal in rhythm.
- JVP: Normal.
- BP: 90/80 mmHg (low systolic, normal diastolic and narrow pulse pressure).

On inspection:

- Visible cardiac impulse in mitral area (or nothing significant).

On palpation:

- Apex beat: In left ... intercostal space, ... cm from midline, heaving in nature.
- Systolic thrill: Present in aortic area, radiates to the right side of neck.

On auscultation:

- First heart sound: Normal in all the areas.
- Second heart sound: A2 is soft in all areas and P2 is normal.
- There is a harsh ejection systolic murmur in aortic area, which radiates to right side of neck.
- May be reversed splitting of second heart sound, and fourth heart sound may be present.

My diagnosis is AS.

Q: What are your **differential diagnoses**?
A: As follows:

- PS.
- HCM.

Q: **Why not** PS?
A: In PS, findings are:

- Systolic thrill in pulmonary area.
- Left parasternal lift and epigastric pulsation may be present (due to RVH).
- P2 is soft, A2 is normal (wide splitting of the second heart sound may be present).
- Ejection systolic murmur in pulmonary area, which radiates to the left side of neck (murmur is more on inspiration).
- Apex is normal (not heaving as in AS).

Q: **Why not** HCM?
A: In HCM, the findings are:

- Pulse is jerky.
- Prominent **'a'** wave in JVP.
- Double impulse at the apex (palpable fourth heart sound due to left atrial hypertrophy).
- Systolic thrill in left lower parasternal area.
- Associated PSM due to MR.
- Family history of HCM may be present or there may be history of sudden death in family.

N.B. In HCM, echocardiography is very helpful for diagnosis. ECG shows LVH and bizarre abnormalities like pseudoinfarction pattern, deep T-wave inversion.

Q: Does the **loudness** of murmur indicates severity?
A: No, prolongation of murmur indicates severity. Loudness of murmur may be associated with mild stenosis.

Q: What is the **type of pulse** in AS?
A: Plateau or anacrotic pulse is slow rising, may be small-volume pulse (pulsus parvus) or late peaking (pulsus tardus).

Q: **Why** anginal pain occurs in AS?
A: There is left ventricular hypertrophy, so there is more oxygen demand. Also, there is reduced coronary flow due to less cardiac output (limitation of duration of diastole).

Q: What are the **signs of severe** AS?
A: Signs of severe AS are:

- Pulse is feeble or absent. Slow rising plateau pulse may be present.
- Systolic aortic thrill.
- Absent or soft A2 (or single S2).
- Harsh, loud, prolonged murmur with late peaking (soft and short ESM with early peaking suggest mild stenosis).
- Reversed splitting of second heart sound.
- Presence of fourth heart sound.
- Presence of heart failure or LVF (late sign).

N.B. Also remember the following points:
- Normal area of aortic valve is 1.5–2 cm^2. It is severe, if the area is <1 cm^2 or valve mean pressure gradient is >50 mmHg.
- Critical AS: If the valve area is <0.7 cm^2 or valve pressure gradient is >70 mmHg.

Q: What are the **complications** of aortic stenosis?

A: As follows:
- LVF.
- Infective endocarditis (10% cases).
- Sudden death due to ventricular fibrillation.
- Complete heart block (in case of calcification of aortic valve).
- Systemic embolism.

Q: What are the **causes** of aortic stenosis?

A: As follows:
- Chronic rheumatic heart disease.
- Bicuspid aortic valve (common in male).
- Calcification in old age.
- Congenital (in early age).

Cause of aortic stenosis according to age:

- **Infants, children and adolescents:**
 - Congenital aortic stenosis.
 - Congenital subvalvular aortic stenosis.
 - Congenital supravalvular aortic stenosis.
- **Young adults to middle-aged:**
 - Calcification and fibrosis of congenitally bicuspid aortic stenosis.
- **Middle-aged to elderly:**
 - Senile degenerative aortic stenosis.
 - Calcification of bicuspid valve.
 - Rheumatic aortic stenosis.

Remember the following points in elderly patient:

- AS is the most common form of valve disease in old age.
- It is a common cause of syncope, angina and heart failure in this age group.
- Low pulse pressure and slow rising pulse may not be present due to stiffening of the arteries.
- Surgery can be successful in the absence of comorbidity, but operative mortality is higher. Prognosis is poor in symptomatic patients without surgery.
- Biological valve is more preferable than mechanical valves. Anticoagulant is not needed.

Q: What are the **types** of AS?

A: There are three types of AS, viz.:
- Valvular (involving valve cusps).
- Subvalvular (membranous diaphragm or fibrous ridge just below the aortic valve).
- Rarely, supravalvular (narrowing in ascending aorta or fibrous diaphragm just above aortic valve). It may be associated with characteristic face such as broad forehead, widely set eyes and pointed chin, mental retardation and hypercalcaemia called William syndrome.

Q: What is **aortic sclerosis**? How to **differentiate** it from AS?

A: It is a degenerative condition characterised by thickening of aortic valve cusps. It is common in the elderly. This does not produce any obstruction to the outflow of blood.

	Features	Aortic stenosis	Aortic sclerosis
1.	Pulse volume	Low, slow raising	Normal
2.	Apex beat	Heaving	Normal
3.	Thrill	Systolic	No thrill
4.	A2	Absent or soft	Normal
5.	ESM	Present, and radiates to the neck	Present, usually no Radiation

N.B. Risk of aortic sclerosis: There may be calcification leading to AS. There are some risk factors like hyperlipidaemia, diabetes mellitus, smoking, hypertension, which make a person prone to develop aortic calcification.

Q: What are the **presentations** of aortic stenosis?

A: As follows:
- Asymptomatic in mild case.
- Breathlessness, mostly on exertion.
- Palpitation.
- Syncope during effort (due to inadequate cardiac output or reflex vasodilatation after exercise or dysrhythmia, causing cerebral hypoperfusion).
- Angina (in 50% cases with or without coronary artery disease).
- Sudden death (probably due to ventricular fibrillation).
- In elderly may be associated with complete heart block or LBBB.

Q: What **investigations** do you suggest in AS?

A: As follows:
- X-ray chest (may be normal in early case. Enlarged left ventricle and dilated ascending aorta, calcification of valve on lateral view).

- ECG (LVH, may be LBBB, complete AV block due to calcification of ring may be found).
- Echocardiogram, preferably colour Doppler echo.
- Cardiac catheterization (mainly to identify associated coronary artery disease. Also to measure the gradient between left ventricle and aorta).

Q: What is the **role of ETT** in AS?

A: ETT should be avoided in symptomatic patient with AS, as it may be fatal. However, it can be done in asymptomatic cases with high-grade AS. ETT may be helpful in deciding the role of surgery.

Q: How to **treat** aortic stenosis?

A: As follows:

- In mild or asymptomatic cases and if valvular pressure gradient <50 mmHg: Follow-up (periodic echocardiogram should be done). Conservative symptomatic management is given.
- If symptomatic or even single syncopal attack: Immediate valve replacement.
- In asymptomatic patient with severe AS and a deteriorating ECG: Valve replacement is also recommended.
- If the patient is unfit for surgery, percutaneous valvuloplasty may be attempted.
- Aortic balloon valvuloplasty is useful in congenital AS. But this is of no value in old age with calcific AS (valve replacement is necessary in such cases).
- In children, elderly or pregnancy: Valvotomy may be done.
- Anticoagulant is only necessary if there is associated atrial fibrillation or mechanical valve prosthesis is used.

Q: Which prosthetic valve is **preferred** in elderly patient?

A: Usually biological or tissue valve is preferred than mechanical one, as biological valve does not require anticoagulation. In younger age, mechanical valve is preferred, but anticoagulant should be given.

Q: What are the **indications of surgery**?

A: As follows:

- All symptomatic patients (such as syncope).
- If mean systolic pressure gradient is >50 mmHg (left ventricular systolic pressure > aorta).
- If the valve area is <0.7 cm^2 (normal: 2.5–3 cm^2).
- Asymptomatic patient undergoing surgery for coronary disease, other valve, LV dysfunction, progressive decline in LVEF, marked LVH.
- Abnormal BP in response to exercise.
- VT.

Q: If the patient with AS has **bleeding** per rectum, what is the likely underlying cause?

A: Angiodysplasia of the colon (Heyde syndrome).

Aortic Regurgitation

Usual instructions are:

- Examine the precordium. Or, palpate and auscultate the precordium.

Presentation of a Case

- Pulse: 92/min, high volume, collapsing type, normal in rhythm.
- JVP: Normal.
- There is dancing carotid pulse in the neck (Corrigan sign).
- BP: 180/55 mmHg (high systolic, low diastolic and wide pulse pressure).

On inspection:

- Visible cardiac impulse (may or may not be).

On palpation:

- Apex beat: In left ... intercostal space, ... cm from midline, thrusting in nature.
- Thrill: Present in left parasternal area, diastolic in nature (patient sitting and bending forward).

On auscultation:

- First heart sound: Normal in all the areas.
- Second heart sound: A2 is absent and P2 is normal.
- There is an EDM which is high pitched, blowing, best heard in left lower parasternal area in third or fourth intercostal space, with patient bending forward and breathing held after expiration.

N.B. Mention, if the following findings are present:

- Ejection systolic murmur in aortic area, which radiates to right side of neck.
- An MDM called Austin Flint murmur.
- Duroziez murmur (over the femoral artery).
- Capillary pulsation (seen in nail bed, inner side of lip, fundus during ophthalmoscopy).

My diagnosis is **aortic regurgitation.**

Q: What is your **differential diagnosis**?
A: Pulmonary regurgitation (PR).

Q: How to **differentiate** AR from PR?
A: In PR, findings are:
- Early diastolic murmur in pulmonary area (called Graham Steel murmur), which is more prominent on inspiration.
- Evidence of PH may be present (e.g. palpable P2, left parasternal heave, epigastric pulsation, etc.).

N.B. PR is rare as an isolated phenomenon, usually associated with pulmonary artery dilatation due to PH, secondary to other diseases (e.g. MS).

Q: Mention one investigation to confirm your diagnosis.
A: Echocardiography, preferably colour Doppler.

Q: What **investigations** do you suggest in this case?
A: As follows:
- X-ray chest (cardiomegaly, dilated ascending aorta, pulmonary oedema).
- ECG (LVH).
- Echocardiogram, preferably colour Doppler.
- Cardiac catheterization.
- Other investigations to find out the cause according to the clinical suspicion.

Q: Why is it called **Water hammer pulse**?
A: The name was originated from a Victorian toy, 'Consisted of a sealed tube, half filled with water and half being vacuum. Inversion of the tube causes the fluid to fall rapidly without air resistance and strike the other end with a noise like hammer blow'.

N.B. To diagnose AR, remember the formula of three:
- **Three pulse:** Collapsing or water hammer, dancing carotid and capillary pulsation.
- **Three BP:** High systolic, low diastolic and wide pulse pressure.
- **Three murmur:** EDM, Austin Flint murmur and Duroziez murmur.

Q: In AR, what **other signs** are to be seen (if asked to examine precordium only)?
A: As follows:
- BP (see above).
- Quincke sign: Capillary pulsation at nail bed (alternate flushing and paleness of skin at the root of nail while pressure is applied at the tip of nail). It may be normally present and better seen with glass slide.
- de Musset sign: Head nodding with each heart beat (with each pulse).
- Duroziez sign: Usually diastolic (may be systolic) murmur over femoral artery on gradual compression of the artery and auscultated proximally.
- Pistol shot murmur: May be heard over femoral artery (Traube sign).
- Hill sign: Higher BP in legs than arms (systolic) and indicates severe AR.
- Mueller sign: Pulsation in uvula with heart beat. (Most of the signs are rare and unhelpful.)

Q: What will you look for in the **eyes and mouth** in AR?
A: As follows:
- Eye: Argyll Robertson pupil (syphilis), dislocated lens, irregular pupils and iridodonesis (Marfan syndrome).
- Mouth: High-arched palate (Marfan syndrome).

Evidence of ankylosing spondylitis and rheumatoid arthritis.

Q: What are the **causes of wide pulse pressure**?
A: As follows:
- AR.
- PDA.
- AV fistula.
- Hyperdynamic circulation (thyrotoxicosis, anaemia, beriberi and pregnancy).

Q: What are the **causes of EDM**?
A: As follows:
- AR.
- Pulmonary regurgitation (signs of PH are present and other peripheral signs of AR are absent).

Q: Why ESM in AR?
A: Due to increased flow through aortic valve without AS (or may be associated with AS).

Q: Why MDM in AR (Austin Flint murmur)?
A: Due to regurgitant flow from aortic valve causing vibration of anterior leaflet of mitral valve.

Q: Why is this MDM **not** due to MS?
A: In MS, there should be:
- Tapping apex beat.
- Loud first heart sound.
- MDM associated with presystolic accentuation.
- Opening snap.

Q: What are the **signs of severe AR**?
A: Signs of severe AR:
- Prolonged EDM.
- A2 absent or soft.
- Presence of left ventricular third heart sound.
- Presence of Austin Flint murmur.
- Signs of LVF.
- Signs of enlarging heart.

Q: What are the **causes** of angina in AR?

A: As follows:

- Low diastolic BP compromise the coronary perfusion pressure causing angina.
- Marked compensatory LVH.

Q: What are the **causes of AR**?

A: As follows:

- Chronic rheumatic heart disease.
- Infective endocarditis.
- Syphilitic aortitis.
- Bicuspid aortic valve.
- Dissecting aneurysm affecting ascending aorta.
- Hypertension (by aortic dilatation).
- Marfan syndrome.
- Seronegative arthritis (ankylosing spondylitis, Reiter syndrome).
- Rheumatoid arthritis.
- Cystic medial necrosis.
- Congenital.

Cause of AR according to the site or abnormality:

1. **Due to involvement of valve:**
 - Rheumatic fever.
 - Infective endocarditis.
 - Bicuspid aortic valve.
 - Trauma.
2. **Aortic root dilatation:**
 - Marfan syndrome.
 - Dissecting aneurysm affecting ascending aorta.
 - Syphilitic aortitis.
 - Hypertension.
 - Trauma.
 - Seronegative arthritides (ankylosing spondylitis, Reiter syndrome, psoriatic arthropathy).
 - SLE.
 - Rheumatoid arthritis.
 - Pseudoxanthoma elasticum.
 - Osteogenesis imperfecta.
 - Rare causes: Appetite suppressants (like fenfluramine, phentermine).

Q: What are the **causes of acute AR**?

A: As follows:

- Acute bacterial endocarditis.
- Acute RF (due to valvulitis).
- Dissecting aneurysm affecting ascending aorta.
- Trauma.

N.B. In acute AR, there is soft, short, early diastolic murmur with diastolic thrill. Most patients have heart failure. Peripheral signs and cardiomegaly are absent. It should be treated by emergency surgery.

Q: How to **differentiate** between AR of rheumatic origin and due to other causes?

A: In rheumatic origin:

- History of rheumatic fever.
- Other valvular lesion, commonly mitral.
- Echocardiogram, if there is thickening and shortening of cusps, fusion of commissure.

(If AR is due to **other causes,** there is dilatation of aorta or valve ring.)

Q: How to **differentiate** syphilitic AR and rheumatic AR?

A: As follows:

	Features	Syphilitic AR	Rheumatic AR
1.	Age	>40 years	Early age
2.	History of	Syphilis	Rheumatic fever
3.	EDM	In aortic area	In left lower parasternal
4.	Peripheral signs	Usually absent	Present
5.	Lesion	Only AR and never AS	Both may be present
6.	Echocardiogram	No cusp involvement	Cusp involvement
7.	Aorta	Dilated, and calcification may occur	No calcification

N.B. Syphilis never causes AS, only aortic regurgitation.

Q: How to **treat** AR?

A: As follows:

1. In asymptomatic moderate to severe AR with normal LV function: Long-acting nifedipine.
2. In symptomatic patient with:
 - Normal LV function: Long-acting nifedipine.
 - LV dysfunction: Digitalis, ACE inhibitor, diuretic.
 - Heart failure: Digitalis, ACE inhibitor, diuretic.
3. In severe case: Valve replacement.

Indications of surgery:

1. Symptomatic patient.
2. Asymptomatic patient with:
 - LV systolic dysfunction (EF <50%)
 - LV dilatation (LV end systolic dimension >55 mm or LV end diastolic dimension >75 mm).
 - Aortic root dilatation >50 mm.

N.B. The valve should be replaced before significant left ventricular dysfunction occurs.

Aortic Stenosis with Aortic Regurgitation (Mixed Aortic Valve Disease)

Usual instructions are:

- Examine the precordium. Or, palpate and auscultate the precordium.

Presentation of a Case (Predominant AS): Case No. 1

- Pulse: 100/min, low volume and slow rising, normal in rhythm, pulsus Bisferiens is present (in carotid).
- JVP: Normal.
- BP: Low systolic and normal diastolic, narrow pulse pressure.

On inspection:

- Visible cardiac impulse (may or may not be).

On palpation:

- Apex beat in left ... intercostal space, ... cm from midline, heaving in nature.
- Systolic thrill: Present in aortic area, radiates to the right side of neck.

On auscultation:

- First heart sound: Normal in all the areas.
- Second heart sound: A2 is soft or absent and P2 is normal.
- There is an ejection systolic murmur in aortic area, which radiates to the right side of neck and also there is an EDM in the left lower parasternal area.

My diagnosis is **AS with aortic regurgitation.**

Q: Which one is the **predominant** lesion and why?
A: Predominant lesion is AS because:

- Pulse: Low volume and slow rising.
- BP: Low systolic, normal diastolic and narrow pulse pressure.
- Apex beat is heaving.
- Systolic thrill in aortic area.
- A2 is absent.

Q: What are the findings, if **AR is predominant**?
A: If AR is predominant, then:

- Pulse: High volume and collapsing.
- Apex beat: Shifted and thrusting.
- BP: High systolic, low diastolic and wide pulse pressure.

Q: What is your **differential** diagnosis?
A: There is combined systolic and diastolic murmur. So this may be confused with conditions that present with continuous murmur like:

- PDA (murmur is called machinery murmur or train in a tunnel)
- Pulmonary arteriovenous fistula.
- PS with pulmonary regurgitation.

Q: What is the likely **cause**?
A: As follows:

- Chronic rheumatic heart disease.
- Congenital bicuspid aortic valve.

Q: Could it be due to **syphilis**?
A: No, syphilis never causes AS.

Q: How to **treat** the case?
A: As follows:

- In mild-to-moderate case, follow-up and prophylactic penicillin to prevent endocarditis are suggested.
- In severe case, valve replacement is required.

Presentation of a Case (Predominant AR): Case No. 2

Present as in Case no. 1 **except:**

- Pulse: High volume and collapsing in nature.
- BP: High systolic, low diastolic and wide pulse pressure.
- Apex beat: Shifted and thrusting in nature.

My diagnosis is **aortic regurgitation with** AS.

Q: Which one is **predominant**?
A: AR is predominant (see above).

Q: Could it be **purely** AR without stenosis?
A: Yes, ESM may be found in AR due to increased flow through aortic valve without AS.

Q: What **investigations** do you suggest?
A: As follows:

- X-ray chest.
- ECG (LVH).
- Echocardiogram, preferably colour Doppler.
- Cardiac catheterization.

Q: How to **treat** the case?
A: As follows:

- In mild-to-moderate case: Follow-up.
- In severe case: Valve replacement.

Tricuspid Regurgitation (TR)

It is unusual to get pure TR. Often there is an association with other valvular lesion (e.g. MS with TR or MS and MR with TR). Whenever you get MS or MR, look carefully to find any evidence of TR.

Usual instructions are:

- Examine the precordium. Or, palpate and auscultate the precordium.

Presentation of a Case: Pure TR

- Pulse: 74/min, normal in volume, rhythm and character.
- JVP: Raised, there is giant V-wave oscillating up to ear lobule.

On inspection:

- There may be nothing significant.

On palpation:

- Apex beat: In left ... intercostal space, ... cm from midline, normal character.
- Thrill: Absent.
- Left parasternal lift and epigastric pulsation are present.

On auscultation:

- First heart sound: Soft in tricuspid area, and normal in other areas.
- Second sound: Normal in all the areas.
- There is a PSM in left lower parasternal area, no radiation and louder with inspiration.
- MDM may be present, louder with inspiration, due to increased flow through tricuspid valve.

My diagnosis is TR.

Q: What **else** do you want to see?

A: Liver: Enlarged, tender and pulsatile (Occasionally ascites, oedema and pleural effusion may occur in TR; right nipple may dance with heart beat. In leg, dilated pulsatile veins may be present rarely).

N.B. Cardinal findings in TR:

- Prominent V-wave in JVP.
- PSM in left lower parasternal area, louder with inspiration (Carvallo sign) and reduce in expiration or during Valsalva manoeuvre.
- Liver: Enlarged, tender and pulsatile.

Q: What is your **differential diagnosis**?

A: MR.

Q: What are the **differences** between TR and MR?

A: As follows:

MR	TR
1. PSM in mitral area	PSM in left lower parasternal area
2. PSM radiate to left axilla	No radiation
3. Murmur increases with expiration	Murmur increases with inspiration
4. No pulsatile liver	Pulsatile liver
5. No V-wave in JVP	V-wave in JVP

Q: What are the **causes** of TR?

A: As follows:

- Functional (PH, cor pulmonale, right heart failure).
- Chronic rheumatic heart disease (usually associated with mitral or aortic valve disease).
- Infective endocarditis (right heart commonly involved in drug addicts).
- Congenital heart disease (Ebstein anomaly).
- Carcinoid syndrome.

Right ventricular papillary muscle infarction, trauma or steering wheel injury in chest.

Q: What are the **causes of pulsatile liver**?

A: As follows:

- TR (the commonest cause).
- Arteriovenous (AV) fistula.
- Angioma of liver (rare).
- Presystolic pulsation in PS.

Q: What is the **commonest** cause of TR? How to treat TR?

A: Functional (secondary to dilatation of right ventricle in PH, cor pulmonale or right heart failure).

Treatment:

- Treatment of primary cause.
- In severe organic TR, operative repair (annuloplasty or plication) is suggested. Occasionally, valve replacement is needed.

Q: What is **Ebstein anomaly**?

A: It is a congenital heart disease associated with downward displacement of tricuspid valve into the right ventricle. Hence, right atrium is large and right ventricle is small. Characteristically, multiple clicks occur due to asynchronous closure of tricuspid valve. ASD is commonly associated with this anomaly.

Pulmonary Stenosis (PS)

Usual instructions are:

- Examine the precordium. Or, palpate and auscultate the precordium.

Presentation of a Case

(Usually, the patient is an adult or elderly)

- Pulse: 70/min, normal in volume, rhythm and character.
- JVP: Normal (may be raised with prominent 'a' wave due to RAH).

On inspection:

- Nothing significant.

On palpation:

- Apex beat: Palpable in left ... intercostal space, ... cm from midline.
- Left parasternal lift and epigastric pulsation (due to RVH).
- Systolic thrill: Present in pulmonary area.

On auscultation:

- First heart sound: Normal in all the areas.
- Second heart sound: P2 is soft in pulmonary area and A2 is normal (wide splitting of the second sound may be present).
- There is a harsh ejection systolic murmur in pulmonary area, which radiates to the neck (more on inspiration). Murmur may be preceded by ejection click.
- Fourth heart sound may be present (due to right atrial contraction).

My diagnosis is **PS.**

Q: What are the **causes of PS?**
A: As follows:

- Congenital (the commonest cause).
- Associated with Carcinoid syndrome.
- Associated with Noonan syndrome.
- Associated with Fallot tetralogy.
- Rarely, in chronic rheumatic heart disease.

N.B. PS may occur, if there is rubella in pregnancy.

Q: What are the **signs** of severe PS?
A: Signs of severe PS:

- P2 is absent; and there is wide splitting of second heart sound.
- Murmur is prolonged, loud and harsh.
- Left parasternal lift (RVH).
- ECG shows RVH and RAH.
- Chest X-ray shows poststenotic dilatation of pulmonary artery.

Q: What are the **clinical presentations** in PS?
A: As follows:

- May be asymptomatic.
- Symptoms such as fatigue, weakness and effort syncope may occur.
- Other features include cyanosis, right ventricular failure and dysrhythmia (AF).

Q: What are the **types** of PS?
A: There are three types, viz.:

- Valvular.
- Subvalvular.
- Supravalvular.

Q: What are the **complications** of PS?
A: As follows:

- Right heart failure.
- Pulmonary embolism (no systemic).

N.B. Infective endocarditis is unusual in PS. Prophylactic antibiotic is unnecessary.

Q: What are the **radiological findings** in PS?
A: It shows:

- Enlarged pulmonary conus, with poststenotic dilatation (in valvular stenosis).
- Oligaemic lung fields.

Q: How to **treat** PS?
A: As follows:

- In mild case, compatible with normal life (no specific treatment).
- In severe symptomatic case, when the pressure gradient is >50 mmHg, balloon valvuloplasty is the treatment of choice.

Prosthetic Heart Valves

(**Remember:** There is a vertical midsternal scar mark. Think of either valve replacement or CABG. In metallic valve replacement, there is metallic sound on auscultation; and in tissue valve replacement, and there is click.)

Usual instructions are:

- Examine the precordium. Or, palpate and auscultate the precordium.

Presentation of a Case:

- Present the case starting from pulse, JVP as described before.

Add the following points:

Case No. 1

- There is a midsternal scar.
- On auscultation, a metallic sound in mitral area that coincides with first heart sound.
- Second sound is normal.
- There is a metallic opening snap.

My diagnosis is **metallic mitral valve prosthesis.**

Case No. 2

- There is a midsternal scar.
- On auscultation, there is a metallic sound in aortic area that coincides with the second heart sound.
- First heart sound is normal.
- There is a metallic opening snap.

My diagnosis is **metallic aortic valve prosthesis.**

Q: What happens, if **there is tissue** valve?

A: In tissue valve prosthesis, no metallic sound or plopping sound is present. The click is present.

Q: What are the **types** of prosthetic valve?

A: Prosthetic valves are of two types:

1. **Metallic valves:**
 - Starr–Edwards valve (ball–cage valve).
 - Bjork–Shiley valve (tilting disc).
 - St. Jude valve (bi-leaflet, double tilting disc).
2. **Tissue valves:**
 - Carpentier–Edwards valve.
 - Hancock porcine valve.
 - Ionescu–Shiley valve (less used).

N.B. Tissue valve—two types:

- Xenograft: Made from porcine valve or bovine pericardium. These are less durable and may require replacement after 8–10 years. Anticoagulation is not required unless there is AF.
- Homograft: These are cadaveric valves (aortic or pulmonary human valve). They are particularly useful in young patient and in the replacement of infected valves.

Q: How to **detect** that the patient has prosthetic valves?

A: It is detected in the following ways:

- Usually there is a vertical midsternal scar mark of thoracotomy. (It may also be due to CABG.)
- In metallic valve replacement, there is metallic sound on auscultation. However, modern mechanical valve (St. Jude valve) makes softer opening and closing sound than older valves.
- In case of tissue valve prosthesis, there is no metallic sound or plopping sound. Rather, there is a click.

Q: How to **detect clinically** whether the replaced valve is mitral or aortic?

A: As follows:

1. **Mitral valve prosthesis is detected by:**
 - Site: Over the mitral valve.
 - Metallic sound is present, coincides with first heart sound (sharp closing).
 - Normal second heart sound.
 - Diastolic flow murmur (MDM) may be present normally.
 - Sharp opening or closing sound or click that coincides with the carotid pulse.
2. **Aortic valve prosthesis is detected by:**
 - Site: Over the aortic valve.
 - Metallic sound is present, coincides with second heart sound (sharp closing).
 - Normal first heart sound. Ejection systolic murmur (ESM) may be present normally.
 - Sharp opening or closing sound or click that occurs shortly after the carotid pulse.

N.B. Mostly Starr–Edwards valve is used.

Q: How to **detect**, if prosthetic valve is **leaking**?

A: As follows:

- In mitral valve prosthesis: Appearance of PSM indicates leaking (MDM may be normally present. Ball–cage valves project into the left ventricle and cause a low-intensity ESM. Tissue

valve and bi-leaflet valve can have a low-intensity diastolic murmur. Consider any systolic murmur of loud intensity to be a sign of regurgitation and failure of the valve.).

- In aortic valve prosthesis: Appearance of EDM indicates leaking. (ESM may be normally present as all types of valves produce a degree of outflow obstruction, and thus have an ESM.)

Q: What happens, if there is **dysfunction** of prosthetic valve?

A: Absence of opening and clicking or closing sounds indicates dysfunction. Unexplained heart failure may be due to dysfunction. Biological valve dysfunction is usually associated with regurgitant murmur.

Q: What are the **advantages and disadvantages** of different valves?

A: As follows:

1. **In case of metallic valve:**
 - Advantage: Incidence of valve failure is less and more durable.
 - Disadvantage: Incidence of thrombosis is usually high, requiring long-time anticoagulant therapy, even life-long. There may be microangiopathic haemolytic anaemia.
2. **In case of tissue valve:**
 - Advantage: Incidence of thrombosis is less; hence, long-time anticoagulant therapy is not required (short-term anticoagulant is used in postoperative period. Also, anticoagulant is required, if associated with AF). No haemolysis.
 - Disadvantage: Incidence of valve failure is high due to stiffening and later tearing of valve leaflets over 10 years, and requires repeat valve replacement and is less durable. There is degeneration and calcification in advanced stage.

Q: What are the **complications** of metallic valve?

A: As follows:

- Thromboembolism.
- Anticoagulation is needed, which may lead to bleeding.
- Microangiopathic haemolytic anaemia
- Infective endocarditis.

Q: What are the **complications** of tissue valve?

A: As follows:

- Primary valve failure.
- Perforation or rupture.
- Degenerative changes.
- Calcification.
- Infective endocarditis.

Q: What are the **complications** of prosthetic valve?

A: As follows:

- Thromboembolism: More on metallic valve (common in mitral than aortic). Anticoagulant is necessary (INR should be between 3 and 4.5).
- Primary valve failure: Rare in metallic valve (common in tissue valve).
- Valve leaking.
- Dehiscence or detachment of valve from the site or valve ring resulting in paraprosthetic leak.
- Valve obstruction by thrombosis or calcification.
- Mechanical or microangiopathic haemolytic anaemia (mainly in aortic valve in 10–20% in 10 years. Occurs due to metallic valve).
- In tissue valve, there may be perforation, rupture and degenerative changes due to calcium deposition.
- Infective endocarditis, especially in dental procedure or catheterisation. Common organism is *Staphylococcus epidermidis*. Occasionally, treatment may be difficult, may cause high mortality and may require replacing the valve again. If infection occurs within 60 days of valve replacement (early), it is mostly by contamination of intravenous (IV) cannula; and if the infection occurs after 60 days (late), it is like other valve endocarditis.

N.B. Remember the following points:

- Ball–cage valve causes haemolysis more than other valve.
- Tilting disc is more thrombogenic.

Q: How to **choose** a particular valve?

A: In the following way:

- In young patients, if no contraindication for anticoagulant therapy, metallic valve prosthesis is preferred.
- In elderly patient or if there is contraindication to anticoagulant therapy, tissue valve prosthesis is preferred.

Q: Which prosthesis is used in a **woman at childbearing age?**

A: Mechanical valves are now preferred for woman at childbearing age. During pregnancy, warfarin is substituted with IV unfractionated heparin in the first 6–12 and last 2 weeks. This is associated with a low rate of warfarin embryopathy and that of bleeding. Subcutaneous heparin and low-molecular-weight heparin are not recommended at present.

Recent studies have showed that women who need low doses of warfarin (5 mg or less) are at low risk for fetal warfarin embryopathy, bleeding,

stillbirth or abortion. In these women, warfarin may be given throughout pregnancy but should be closely monitored.

Previously tissue valve was used for young woman considering the risk of anticoagulation at pregnancy. But with tissue valve, there is increased risk of early structural valve deterioration (SVD) during or shortly after the end of pregnancy. In addition, tissue valve is less durable and repeat valve replacement may be needed after about 10 years.

Congenital Heart Disease

Common congenital heart diseases are described in this chapter. Usual cases selected in the examination are **VSD** (see page 95), **ASD** (see page 98), PDA (see page 99), **Fallot tetralogy** (see page 93), **coarctation of aorta** (see page 106). Others **PS** (see page 89), TR (see page 88) are sometimes selected; for details see the aforementioned topics on the given pages.

A Brief Note on Congenital Heart Diseases

Any defect or malformation in one or more structures of the heart or blood vessels that occurs during pregnancy is called congenital heart disease. It affects about 1 in 100 babies. This may remain asymptomatic, or symptoms may appear after birth, at childhood or in adult.

Causes of Congenital Heart Diseases

Actual cause is unknown; but some factors may increase the risk of congenital heart disease. These are:

- Genetic abnormality (e.g. Marfan and DiGeorge syndromes).
- Chromosomal abnormalities (e.g. Down syndrome is associated with septal defects, and mitral and tricuspid valve defects; Turner syndrome is associated with coarctation of aorta).
- Maternal alcohol abuse is associated with septal defects.
- Maternal drug abuse or drug treatment and radiation exposure (use of thalidomide during pregnancy may be associated with amelia or paramelia).
- Maternal viral infection, such as rubella in first trimester of pregnancy is associated with PDA, pulmonary valvular and arterial stenosis, and ASD.
- Maternal illness [e.g. SLE, which is associated with congenital complete heart block, diabetes and phenylketonuria].

Types of Congenital Heart Diseases

A. Acyanotic congenital heart diseases (communication between systemic and pulmonary circulation): These are of two types, viz.:

With left-to-right shunt
- ASD.
- VSD.
- PDA.

With no shunt
- Coarctation of aorta.
- Bicuspid aortic valve.
- Congenital AS.
- PS or pulmonary regurgitation.
- Ebstein anomaly.
- Tricuspid valvular disease.

B. Cyanotic congenital heart diseases:
- TOF.
- Eisenmenger syndrome (PH with right-to-left shunt).
- Transposition of great arteries.
- Others: Truncus arteriosus, tricuspid atresia and total anomalous pulmonary venous drainage.

N.B. The commonest congenital heart disease is VSD.

Tetralogy of Fallot (TOF)

Usual instructions are:

- Examine the precordium. Or, palpate and auscultate the precordium.

(Look at the patient carefully. Is there clubbing and central cyanosis?)

Presentation of a Case

(Usually a child)
- Pulse: 80/min, normal in volume, rhythm and character.

- JVP: Normal (may be prominent 'a' wave due to RVH).

On inspection:

- The patient may be short, dyspnoeic, cyanosed, with plethoric face.

On palpation:

- Apex beat: Palpable in left ... intercostal space, ... cm from midline.
- Left parasternal lift and epigastric pulsation (due to RVH).
- Systolic thrill: Present in pulmonary area.

On auscultation:

- First heart sound: Normal in all the areas.
- Second heart sound: P2 is soft or absent in pulmonary area, and A2 is normal.
- There is a harsh ejection systolic murmur in pulmonary area, which radiates to the neck, more on inspiration.

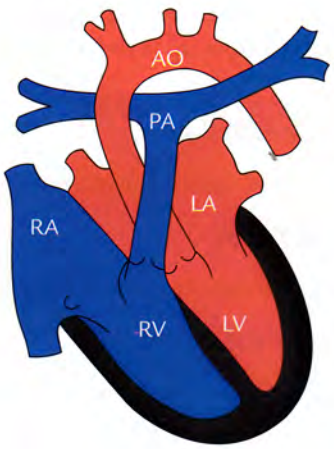
My diagnosis is **TOF.**

Q: What is **TOF?**

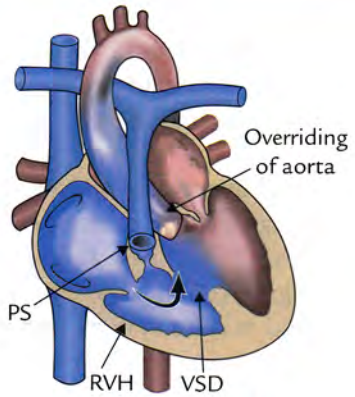
A: It is a cyanotic congenital heart disease consisting of:

- PS.
- Overriding and dextroposition of aorta (aortic origin—two-third from left ventricle and one-third from right ventricle).
- Right ventricular hypertrophy.
- VSD (perimembranous, usually large, subaortic).

N.B. Right ventricular outflow obstruction may be subvalvular (infundibular), valvular or supravalvular. The most common obstruction is subvalvular, either alone (50%) or in combination with PS (25%).



Normal heart



Tetralogy of Fallot

Q: Mention some **cyanotic congenital heart disease.**

A: As follows:

- Tricuspid atresia.
- Transposition of great vessels.
- Pulmonary atresia.
- Ebstein anomaly.

Q: What are the **cardinal features of TOF?**

A: As follows:

- Child with growth retardation.
- Clubbing.
- Cyanosis.
- Pulmonary ejection systolic murmur.
- History of cyanotic spells during exercise (relieved by squatting).

Q: How to assess the **severity** of TOF?

A: As follows:

- Mild case: Loud and prolonged murmur.
- Severe case: Reduced or no murmur.

Q: How the patient usually **presents?**

A: As follows:

- Young children usually present with cyanotic spell (Fallot spell) during exertion, feeding or crying. They may become apnoeic and unconscious.
- In older children, Fallot spells are uncommon but cyanosis becomes increasingly apparent with clubbing and polycythaemia. There may be Fallot sign.
- Shortness of breath on exertion, easy fatiguability.
- Growth retardation.
- Syncope, seizure, cerebrovascular events or even sudden death.

Q: Why **syncope** occurs in TOF during exercise?

A: During exercise, there is increased pulmonary resistance and reduced systemic vascular resistance. Hence, there is increased right-to-left shunt, admixture of blood of right and left ventricle. As a result, there is reduced cerebral oxygenation causing syncope.

Q: Why **cyanosis** in TOF?

A: Because of overriding of aorta, there is admixture of blood of right and left ventricles. Cyanosis is absent in newborn or acyanotic Fallot.

Q: When is cyanosis **aggravated** and why?

A: Cyanosis is aggravated during exercise called cyanotic spell or Fallot spell. It is also aggravated during feeding or crying. Cyanosis is reduced by squatting. Child may be apnoeic and unconscious. Syncope, seizure, cerebrovascular accident (CVA) or sudden death may occur. Fallot spell is uncommon in older children.

Cyanotic spell is due to increased obstruction as a result of increased sympathetic stimulation that occurs during exercise, feeding and crying.

Q: How **squatting** relieves cyanosis?

A: During squatting position, abdominal aorta and femoral artery are compressed. There is increased arterial resistance, so increase pressure at the left ventricular level, diminished right-to-left shunt, increased flow through pulmonary artery, and thereby reduction of admixture of right and left ventricular blood.

Q: Why **no murmur** of VSD in TOF?

A: Because VSD is large, and there is equal pressure in right and left ventricle.

Q: What are the **complications** of TOF?

A: As follows:

- Infective endocarditis (common, 10% cases).
- Paradoxical emboli.
- Cerebral abscess (10% cases).
- Polycythaemia (due to hypoxaemia). It may cause CVA and myocardial infarction.
- Coagulation abnormality.

Q: What **investigations** are done in TOF?

A: As follows:

- Chest X-ray: Boot-shaped heart, pulmonary conus is concave (small pulmonary artery), right ventricle is enlarged (prominent elevated apex), oligaemic lung (right-sided aortic arch in 25% cases).
- 2-D echocardiography and colour Doppler.
- Other investigations: ECG (RVH), cardiac catheterisation in some cases.

Q: How to **treat** TOF?

A: As follows:

- Usually using surgical correction, and ideally using total correction (prior to 5 years of age).
- If pulmonary artery is hypoplastic or anatomy is unfavourable, then temporarily Blalock–Taussig shunt is performed. Corrective surgery is done later on.

Other surgical procedure:

- Modified Blalock–Taussig shunt: Interposition of tubular graft between subclavian and pulmonary artery.
- Pulmonary balloon valvuloplasty.
- Waterston shunt: Anastomosis of the back of the ascending aorta to the pulmonary artery. It is performed when surgery is required under the age of 3 months because the subclavian artery is very small.

Q: What is **Blalock–Taussig** shunt?

A: It is the anastomosis between left subclavian artery and left pulmonary artery. This improves pulmonary blood flow and pulmonary artery development, and may facilitate definitive surgery later on.

Q: **How to detect Blalock–Taussig** shunt at bedside?

A: As follows:

- Thoracotomy scar.
- Left radial pulse: Absent or feeble.
- BP on the left arm: Absent or undetectable.
- Arm on the left side looks smaller than right.

Q: How to **treat** during cyanotic spell?

A: As follows:

- Knee–chest position of child, high concentration of O_2.
- Morphine or diamorphine injection (which relaxes right ventricular outflow obstruction).
- β-blocker.
- If medical therapy fails, emergency surgical shunt may be considered.

Prognosis is good after surgery, especially if operation is done in childhood. After surgery, restenosis, recurrence of septal defect and rhythm disorder may occur. Regular follow-up is required in every case.

Pentalogy of Fallot

- When TOF is associated with ASD.

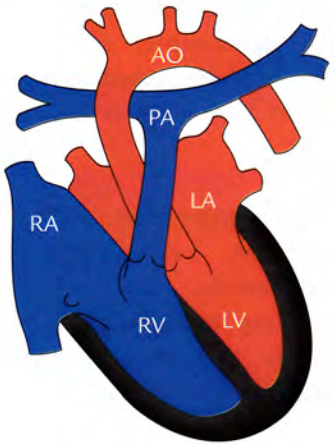
Trilogy of Fallot

- ASD with PS with right ventricular hypertrophy.

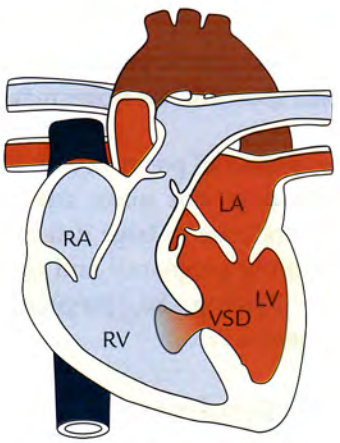
Acyanotic Fallot

- When TOF is associated with infundibular PS. Outflow obstruction is mild and there is no cyanosis.

Ventricular Septal Defect (VSD)



Normal heart



Ventricular septal defect

Usual instructions are:

- Examine the precordium. Or, palpate and auscultate the precordium.

Presentation of a Case

- Pulse: 90/min, normal in volume, rhythm and character.
- JVP: Normal.

On inspection:

- Nothing significant.

On palpation:

- Apex beat: In left ... intercostal space, ... cm from midline, diffuse, thrusting in character.
- Systolic thrill: Present in left parasternal area (fourth or fifth intercostal space).

On auscultation:

- First and second heart sounds are normal in all the areas.
- There is a PSM in left parasternal area in fourth or fifth intercostal space [may be MDM due to increased flow through mitral valve (Third heart sound may be present.)].

My diagnosis is **VSD.**

Q: What are your **differential diagnoses?**
A: As follows:
- MR.
- TR.

Q: **Why not** this is a case of MR?
A: In MR findings are:
- First heart sound is soft.
- PSM in mitral area, which radiates towards the left axilla.

Q: **Why not** this is a case of TR?
A: In TR, findings are:
- JVP may be raised. There may be giant **V**-wave, oscillating up to the ear lobule.
- First heart sound is soft in tricuspid area.
- There is a PSM in left lower parasternal area with no radiation and the murmur is louder with inspiration.
- Also, there may be enlarged, tender, pulsatile liver.

Q: Mention **one investigation** to confirm your diagnosis.
A: Colour Doppler echocardiogram.

Q: What are the **causes** of VSD?
A: As follows:
- Commonly congenital (VSD is the commonest congenital heart disease).
- Acquired rupture of interventricular septum after acute myocardial infarction, rarely trauma.

Q: What is the **site** of VSD?
A: It is commonly seen in the perimembranous part of intraventricular septum (in 90% cases).

Q: Is the **loudness** of murmur related to size of VSD?
A: Small VSD is associated with loud murmur, and large defect is associated with soft murmur.

Q: Does the presentation varies with the **size of VSD**?

A: VSD may be of three types according to the size. These are:

- **Small VSD (Maladie de Roger):** It is asymptomatic and usually closes spontaneously. But, there is a future risk of development of aortic regurgitation or endocarditis even after spontaneous closure. The systolic murmur is loud and prolonged.
- **Moderate VSD:** The patient presents with fatigue and dyspnoea. Heart is usually enlarged with a prominent apex beat. There is often a palpable systolic thrill and a loud 'tearing' PSM at the left lower sternal edge.
- **Large VSD:** The murmur is soft. It may lead to PH, and Eisenmenger complex may result.

Q: What are the **complications of VSD**?

A: As follows:

- Infective endocarditis (more common in small VSD).
- Pulmonary hypertension with reversal of shunt (Eisenmenger syndrome).
- Heart failure.

N.B. When Eisenmenger syndrome develops, there is cyanosis, clubbing and evidence of PH. PSM may disappear because of equalisation of pressure in right and left ventricle.

Q: What **investigations** do you suggest in your case?

A: As follows:

- ECG (LVH, biventricular hypertrophy).
- X-ray chest (cardiomegaly, large pulmonary conus, large hilar arteries, plethoric lung fields).
- Echocardiography, preferably colour Doppler.
- Cardiac catheterization may be necessary in some cases.
- CMR (cardiac magnetic resonance) angiography may be helpful.

Q: What are the **causes** of plethoric lung field?

A: As follows:

- ASD.
- VSD.
- PDA.
- Also in CCF.

Q: How to **treat** VSD?

A: As follows:

1. **If small:** Surgery is not needed; only follow-up should be done. Spontaneous closure may occur in infants, if it is in the muscular part. Prophylactic penicillin for SBE may be given.
2. **Moderate-to-large:** Surgical correction is needed if pulmonary-to-systemic flow ratio >1.5:1. Percutaneous transcatheter closure may be done.
3. **When Eisenmenger syndrome develops:** Surgery is contraindicated, as it aggravates right-sided heart failure. Then following treatments are given:
 - Diuretic.
 - Digoxin in some cases.
 - Venesection, especially if there is polycythaemia.
 - Heart–lung transplantation may be done. Mortality rate is very high than heart transplantation alone.

N.B. VSD may be associated with Turner syndrome, Down syndrome or maternal rubella during pregnancy.

Q: Can VSD be closed **spontaneously**?

A: If small VSD, spontaneous closer may occur.

Q: What is the **impact** of pregnancy on VSD?

A: Small defect does not make any problem with pregnancy. Moderate-to-large defect with PH may get worse during pregnancy and right ventricular failure may develop. So, pregnancy should be avoided if there is PH.

Eisenmenger Syndrome

Usual instructions are:

- Examine the precordium. Or, palpate and auscultate the precordium.

Presentation of a Case

- Pulse: 104/min, low volume.
- JVP: Raised, with prominent 'a' wave.
- BP: 110/70 mmHg.

Precordium:

Inspection:

- Visible cardiac impulse in pulmonary area.

Palpation:

- Apex beat: In the left ... intercostal space, ... cm from midsternal line.
- Left parasternal lift: Present.
- Palpable P2: Present.
- Epigastric pulsation: Present.

Auscultation:

- First heart sound: Normal in all the areas.
- Second heart sound: Louder in all the areas, P2 is accentuated in pulmonary area.
- There is a PSM in the left third and fourth intercostal space, in left parasternal area without any radiation.

My diagnosis is **Eisenmenger syndrome due to VSD.**

Q: What are your **differential diagnoses**?

A: As follows:

- CCF.
- Chronic cor pulmonale.

Q: **Why not** CCF?

A: In CCF, the triad of engorged and pulsatile neck vein, enlarged tender liver and dependant oedema should be present. It is usually secondary to other causes like MS or left-sided heart failure, which are absent in this case.

Q: **Why not this** is a case of chronic cor pulmonale?

A: Cor pulmonale is defined as enlargement of right ventricle with or without failure, which may be due to causes in the lungs parenchyma, pulmonary vessels or chest wall (like kyphosis, scoliosis, etc.). All of these are absent in this case.

Q: What **investigations** do you suggest in this case?

A: As follows:

1. X-ray chest (enlargement of central pulmonary arteries with peripheral pruning of pulmonary vessels).
2. ECG (RVH, RAH, right axis deviation).
3. Echocardiography.

Q: What is **Eisenmenger syndrome**? What are the **causes**?

A: PH with reversal of shunt is called Eisenmenger syndrome. Causes are:

- VSD.
- ASD.
- PDA.

Q: What is **Eisenmenger complex**?

A: PH with reversal of shunt, when due to VSD is called Eisenmenger complex.

Q: What are the **clinical features** of Eisenmenger syndrome?

A: As follows:

- Dyspnoea.
- Fatigue.
- Syncope.
- Angina.
- Haemoptysis.
- Features of CCF.

On examination:

- Central cyanosis (not corrected by giving 100% oxygen). Differential cyanosis (cyanosis in toes, not in the hand) occurs in PDA.
- Clubbing (differential clubbing—clubbing in toes, not in the hand; occurs in PDA).
- Pulse: Low volume.
- Prominent '**a**' wave in JVP.
- Other signs of PH: Palpable P2, left parasternal lift, epigastric pulsation due to RVH. Ejection click and ejection systolic murmur may be present.
- TR may occur (in such case, prominent **V**-wave in JVP; also there may be a PSM in left lower parasternal area).
- Polycythaemia.
- Original murmur of VSD, ASD or PDAL: Decreases in intensity, even may disappear.

N.B. Remember, if any patient is having cyanosis with evidences of PH, the more likely diagnosis is Eisenmenger syndrome.

Q: What are the causes of **death** in Eisenmenger syndrome?

A: As follows:

- Right heart failure.
- Pulmonary infarction.
- Infective endocarditis.
- Cerebral thrombosis or abscess.
- Dysrhythmias.

Q: How to **treat**?

A: As follows:

- Diuretic.
- Digoxin may be given in some cases.
- Venesection may be required, especially if there is polycythaemia.
- Long-term intravenous epoprostenol may be tried.
- Heart–lung transplantation may be done (mortality rate is very high than heart transplantation alone).

Surgery is contraindicated in Eisenmenger syndrome, as it aggravates right sided heart failure.

Q: What is the **effect of pregnancy** in Eisenmenger syndrome?

A: Pregnancy should be avoided as it aggravates right-sided heart failure, early spontaneous abortion. Also, mortality is high in mother.

Atrial Septal Defect (ASD)

Usual instructions are:

- Examine the precordium. Or, palpate and auscultate the precordium.

Presentation of a Case

- Pulse: 86/min, normal in volume, rhythm and character.
- JVP: Normal.
- BP: 120/75 mmHg.

On inspection:

- Nothing significant.

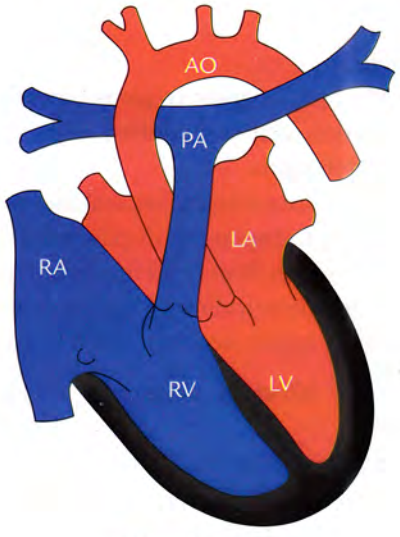
On palpation:

- Apex beat: In left ... intercostal space, ... cm from midline.
- Thrill: Absent.

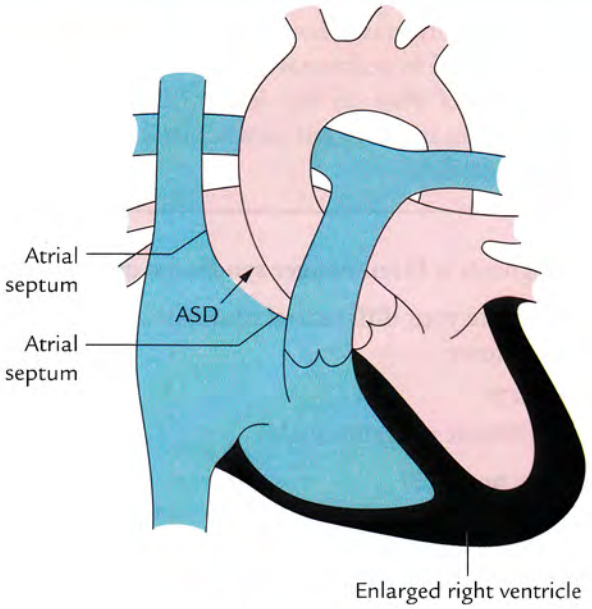
On auscultation:

- First heart sound is normal in all the areas.
- Wide and fixed splitting of second heart sound (very important finding).
- There is an ejection systolic murmur in left second and third intercostal spaces.
- There is (or may be) MDM in tricuspid area.

My diagnosis is **ASD**.



Normal heart



Atrial septal defect

Q: What are your **differential diagnoses**?
A: As follows:

- PS.
- VSD.

Q: **Why not** this is a case of PS?
A: In PS, the findings are:

- Soft or absent P2.
- Thrill present in pulmonary area.
- Wide and fixed splitting of second heart sound is absent.
- ESM may radiate to the neck.

Q: **Why not** this is a case of VSD?
A: In VSD, the findings are:

- Systolic thrill in the left lower parasternal area.
- PSM in the left lower parasternal area.

Q: What is **wide** and **fixed** splitting of second heart sound and why is it **wide** and **fixed** splitting?
A: Wide and fixed splittings mean that it is remaining same in inspiration and expiration.

- Wide because of delay in right ventricular ejection.
- Fixed because of equalisation of pressure between left and right atrium; hence no change in second heart sound with respiration (normally, there is wide splitting during inspiration due to delay of closure of pulmonary valve).

Q: What are the **murmurs** in ASD?
A: The two murmurs are:

- ESM, due to increased flow through pulmonary valve.
- MDM, due to increased flow through tricuspid valve.

(No murmur due to ASD because of equal pressure between left and right atrium.)

Q: What are the **types** of ASD?
A: They are of two types:

- Ostium primum (10% cases) results from atrioventricular defect in septum and there is involvement of AV valve; hence there may be MR or TR.
- Ostium secundum (90% cases) defect mainly at the fossa ovalis.

(ASD is common in females; M:F ratio is 1:2. Ostium primum may occur in Down syndrome.)

Q: What is the **ECG** finding in ASD?
A: ECG shows:

- In primum type, RBBB with left-axis deviation.
- In secundum type, RBBB with right-axis deviation.

Q: What are the **complications** of ASD?
A: As follows:

- PH with reversal of shunt (Eisenmenger syndrome).
- Dysrhythmia (AF, the commonest).
- Embolism (pulmonary and systemic) and brain abscess.

Q: What are the **findings** when there is a reversal of shunt?
A: As follows:

- Both murmurs reduce in intensity.
- P2 is loud.
- Systolic ejection sound is accentuated.
- Other features include PH.

Q: What is **Lutembacher** syndrome?
A: ASD with an acquired rheumatic MS.

Q: What **investigations** do you suggest?
A: As follows:

- Chest X-ray: Cardiomegaly (right ventricle and right atrium are enlarged, also small left atrium and normal aorta), large pulmonary conus, large hilar arteries, lung fields are plethoric (if PH, there is oligaemic lung).
- ECG.
- 2-D echocardiography and colour Doppler, but transoesophageal echo is better.
- Cardiac catheterisation in some cases (fluoroscopy shows hilar dance).
- MRI or CMR may be helpful.

Q: How to **treat** ASD?
A: As follows:

- Small ASD: Surgery is not needed, only follow-up should be done (the patient usually lives a normal life).
- Moderate to large: Surgical closure should be done, if the ratio of pulmonary flow to systemic flow is 2:1 or more.
- Angiographic closure is possible with trans-catheter clamshell device.
- If Eisenmenger syndrome develops: Surgical closer is contraindicated (for other treatment, see in Eisenmenger syndrome).

Q: What is the **effect** of ASD on pregnancy?
A: In uncomplicated ASD, pregnancy is well tolerated. But if Eisenmenger syndrome develops, pregnancy should be avoided because of high maternal and foetal mortality.

Patent Ductus Arteriosus (PDA)

Usual instructions are:

- Examine the precordium. Or, palpate and auscultate the precordium.

Presentation of a Case

- Pulse: 80/min, high volume or collapsing, normal in rhythm.
- JVP. Normal.
- BP: 130/70 mmHg.

On inspection:

- Visible cardiac impulse in apical area and another impulse in pulmonary area.

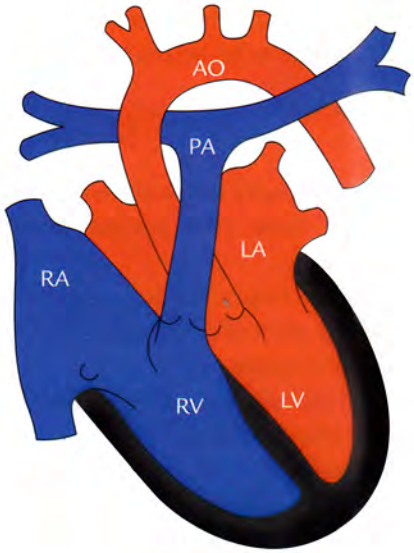
On palpation:

- Apex beat: In left .. intercostal space, ... cm from midline, thrusting or heaving in nature.
- Systolic thrill: Present in pulmonary area (may be diastolic also).
- Pulmonary arterial pulsation may be felt.

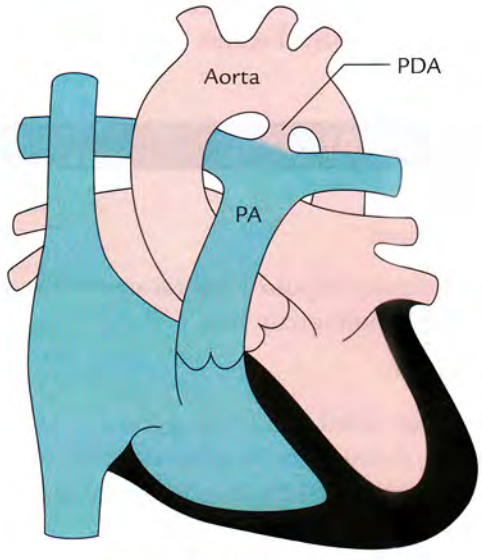
On auscultation:

- First and second heart sounds are normal in all the areas (may be reverse splitting of second heart sound, if large shunt).
- There is a continuous murmur in left second and third intercostal space, more prominent in systole (murmur is prominent on expiration, may be heard posteriorly), and radiates to the neck.
- There may be MDM (due to increased flow).

My diagnosis is **PDA.**



Normal heart



Patent ductus arteriosus

N.B. During foetal life, ductus arteriosus connects pulmonary artery at its bifurcation to the descending aorta just below the origin of left subclavian artery and permits blood flow from pulmonary artery to aorta. After birth, within hours or days, it closes spontaneously and remains as ligamentum arteriosum. In PDA, it allows blood to flow from aorta to pulmonary artery. Up to 50% of left ventricular output may enter into pulmonary artery because pressure in aorta is higher.

Q: What are your **differential diagnoses?**

A: The typical continuous murmur is highly suggestive of PDA. However, any cause of continuous murmur should be excluded such as:

- Arteriovenous fistula (coronary, pulmonary or systemic).
- Venous hum.
- Rupture of sinus of Valsalva to the right ventricle or atrium.

Q: What is **venous hum?**

A: It is a continuous murmur due to kinking and partial obstruction of one of the large veins in the neck. It is found in the neck above the clavicle and upper part of chest, more on the right side of sternum. The hum can be obliterated by pressure on the neck or lying down or altering the position of neck (as there is reduction of venous obstruction). It is accentuated by sitting with head extended and turned to the side opposite to that auscultated. Venous hum has no clinical significance, commonly present in children, should not be confused with any pathology.

Q: What is the **murmur** in PDA?

A: Continuous murmur (machinery murmur like **train in a tunnel**), with late systolic accentuation.

Q: What are the **causes of continuous murmur?**

A: As follows:

- PDA.
- Arteriovenous fistula (coronary, pulmonary or systemic).
- Aortopulmonary fistula (may be congenital or Blalock–Taussig shunt).
- Venous hum.
- Rupture of sinus of Valsalva to the right ventricle or atrium.

Q: What are the **causes** of PDA?

A: Common in females; M:F ratio is 1:3. Probable aetiological factors are:

- Maternal rubella in the first trimester.
- Birth at high altitude with continuous prenatal hypoxia.
- Prematurity.

Q: What are the **findings** in reversal of shunt?
A: As follows:

- Cyanosis and clubbing in lower limb, absent in upper limb (called differential cyanosis or differential clubbing).
- Murmur is quiet or absent or systolic only (diastolic is absent).
- Evidence of PH.

Q: What are the **complications of PDA**?
A: As follows:

- Pulmonary hypertension with reversal of shunt (Eisenmenger syndrome).
- CCF.
- Infective endocarditis.
- Dysrhythmia (AF).
- Duct may rupture or calcify.

Q: What **investigations** do you suggest?
A: As follows:

- ECG (normal, LVH, and RVH in Eisenmenger syndrome).
- Chest X-ray: Cardiomegaly (left ventricle and left atrium are enlarged, also large aorta), large pulmonary conus, large hilar arteries, lung fields are plethoric.
- 2-D echocardiography and colour Doppler echocardiography.
- Cardiac catheterisation may be necessary in some cases.
- Angiography may be done.
- MRI or CMR angiography may be helpful.

Q: How to **treat** PDA?
A: As follows:

- Majority of PDA is small and can be closed at cardiac catheterisation using percutaneously delivered device.
- Surgical closure for large PDA.
- Prophylaxis for infective endocarditis.
- In neonate (1–3 weeks old) indomethacin (0.2 mg/kg IV) may be given, which may constrict and close PDA (by inhibiting prostaglandin E synthesis, and prior to birth, duct is kept patent by the effect of circulating prostaglandin). It is not helpful in older children.
- If Eisenmenger syndrome develops, surgery is contraindicated (see in Eisenmenger syndrome).

Prognosis: If untreated, one-third individuals die from heart failure, PH or endocarditis by the age of 40 and two-third by the age of 60.

Examination of Pulse

The usual instructions are:

- Examine the pulse.
- Examine the pulse and relevants.
- Examine the pulse and auscultate the heart.

Usually **any of the following findings** will be present:

- Irregular pulse (AF and ectopics).
- High-volume pulse or water hammer pulse.
- Bradycardia (complete heart block).
- Unequal radial pulse.
- Absent pulse.
- Radiofemoral delay and radioradial delay or inequality.

(See radial pulse; look for rate, rhythm, volume, character, pulse delay and condition of the vessel wall. Finally, examine all other pulses and compare on both sides).

Q: What are the **causes** of irregular pulse?
A: See page 71.

Q: **Is collapsing** and **high-volume** pulse synonymous?
A: No, collapsing pulse is a high-volume pulse; but all high-volume pulses may not be collapsing.

Q: **If collapsing** pulse is present, what **else** do you want to see?
A: Then it is essential to see the signs of AR:

- BP: High systolic, low diastolic and wide pulse pressure.
- Neck: Dancing carotid pulse.
- Heart: EDM.

Q: What are the **causes** of bradycardia?
A: See page 71.

Causes of unequal radial pulse

- Atherosclerosis (usually elderly).
- Congenital anomaly or aberrant radial artery. Coarctation of aorta (before the origin of left subclavian artery).
- Dissecting aneurysm.
- Takayasu disease.
- Occlusion of subclavian artery (by ribs and neoplasm).
- Aneurysm of aortic arch.
- Iatrogenic (Blalock–Taussig shunt in TOF).

Causes of absent radial pulse

- Anatomical aberration.
- Blockage by embolism or narrowing.
- Takayasu syndrome.
- Iatrogenic (Blalock–Taussig shunt in TOF and AV fistula for haemodialysis).
- Dissecting aneurysm.
- Coarctation of aorta (before the origin of left subclavian artery). Brachial artery catheter with poor technique or tied during surgery.

N.B. Remember, scar mark with thrill in wrist indicates AV fistula for haemodialysis.

Atrial Fibrillation

The usual instructions are:

- Examine the pulse.
- Examine the pulse and relevants.
- Examine the pulse and auscultate the heart.

Presentation of irregular pulse:

- The pulse is 110/min, irregularly irregular (irregular in rhythm and volume).

Q: What are the **causes of irregularly irregular pulse?**
A: As follows:

- Atrial fibrillation.
- Multiple ectopics.
- Others: Atrial flutter with variable block, paroxysmal atrial tachycardia with variable block.

Q: What **else** do you want to see in atrial fibrillation?
A: As follows:

- Heart (heart rate to see pulse deficit, mitral valvular or other cardiac disease).
- Thyroid status (warm sweaty hands, tremor of outstretched hands, tachycardia, exophthalmos and thyroid gland).
- History of **IHD** and BP.
- History of other diseases causing AF (see below).

Q: How to **differentiate** between AF and multiple ectopics in bedside?
A: By physical exercise ectopics will disappear or diminish, but fibrillation will be more prominent or worse (ECG for confirmation, *see below*).

Q: What is the **ECG** in AF?
A: P is absent (P may be replaced by small fibrillary F-wave) and RR interval is irregular.

Q: What are the causes of AF?
A: As follows:

- Chronic rheumatic heart disease, usually with MS.
- IHDs (commonly, acute MI).
- Thyrotoxicosis.
- Hypertensive heart disease.
- Idiopathic or lone AF (10% cases).
- Others include chronic constrictive pericarditis, cardiomyopathy, acute pericarditis, congenital heart disease (ASD), sick sinus syndrome, acute infection (pneumonia), thoracic surgery, electrolyte imbalance (hypokalaemia and hyponatraemia), alcohol abuse and pulmonary embolism.

N.B. Remember the following points:

- First five causes should always be mentioned sequentially at the top of the list.
- Mention the causes of atrial fibrillation according to the age of the patient in that particular long case (see below).

Q: If the patient is **young**, what are the **causes** of atrial fibrillation?
A: As follows:

- Chronic rheumatic heart disease with valvular lesions, commonly MS.
- Thyrotoxicosis.
- Others: Atrial septal defect (ASD), acute pericarditis, myocarditis, pneumonia.

Q: If the patient is **elderly**, what are the **causes** of atrial fibrillation?
A: As follows:

- Coronary artery disease (commonly acute myocardial infarction).
- Thyrotoxicosis.
- Hypertension.
- Lone atrial fibrillation (idiopathic in 10% cases).
- Others: See above (unusual or less in chronic rheumatic heart disease).

Q: What are the **noncardiac causes** of AF?
A: See above.

Q: What is **lone atrial fibrillation?**

A: Lone atrial fibrillation means atrial fibrillation without any cause. Genetic predisposition may be responsible.

- 50% patients with paroxysmal atrial fibrillation and 20% with persistent or permanent atrial fibrillation have no cause and heart is normal.
- Lone atrial fibrillation usually occurs below 60 years of age.
- It may be intermittent, later may become permanent.
- Prognosis: Low risk of CVD (0.5% per year). Usually life span is normal.

Q: What are the **complications** of AF?

A: As follows:

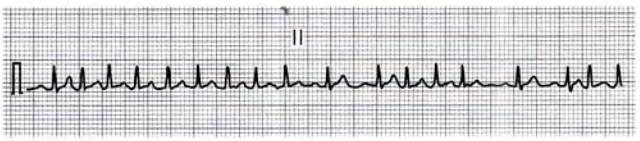
- Systemic and pulmonary embolism (systemic from left atrium and pulmonary from right atrium). Annual risk is 5% (1–12).
- Heart failure.

Q: If a patient with AF is unconscious, what is the likely cause?

A: Cerebral embolism (usually with right-sided hemiplegia).

Q: How to **treat** AF?

A: Assessment with details of history, physical examination and investigation to find out the primary cause. If AF is due to acute illnesses, such as pneumonia, pulmonary embolism and others then the treatment of primary disease will restore sinus rhythm.



ECG of AF

Treatment (according to the type):

1. **Paroxysmal atrial fibrillation:**
 - If asymptomatic: Does not require any treatment, follow-up of the case?
 - If troublesome symptoms are present: β-blocker. Other drugs: Flecainide or propafenone may be given.
 - Amiodarone is effective in prevention.
 - Low-dose aspirin to prevent thromboembolism.
 - If bradycardia is present (in sinoatrial disease): Permanent over drive atrial pacing (60% effective).
 - In some intractable cases: Radiofrequency ablation may be required, who do not have structural heart disease (70% effective).
2. **Persistent atrial fibrillation:**
 - Control of heart rate: β-blocker, digoxin or calcium channel blocker (verapamil, diltiazem). Combination of digoxin and atenolol may be used.
 - To control rhythm: Direct current (DC) cardioversion may be done safely. It may be repeated, if relapse occurs. Concomitant use of β-blocker or amiodarone may be used to prevent recurrence.
3. **Permanent atrial fibrillation:**
 - Control of heart rate: Digoxin, β-blocker, calcium channel blocker (verapamil or diltiazem).
 - In some cases: Transvenous radiofrequency ablation may be done (It induces complete heart block. So, permanent pacemaker should be given. This is known as 'patch and ablate strategy'.)

Q: What is the **role of anticoagulant** in atrial fibrillation?

A: Usually, warfarin is given to those who are at risk of stroke. Target INR is 2–3. It reduces stroke in two-third cases. Aspirin reduces stroke in one-fifth cases. Anticoagulation is indicated in patient with atrial fibrillation having risk factors for thromboembolism.

N.B. Remember the following points:

- In lone atrial fibrillation: Aspirin may be given to prevent thromboembolism.
- Age <65 years and young with no structural heart disease: Aspirin may be beneficial. No warfarin.
- Target INR following anticoagulation is 2–3.

Types of AF

Two types according to heart rate:

- Fast AF (pulse >100/min).
- Slow AF (pulse <100/min).

Three types according to its nature:

- Paroxysmal: Discrete self-limiting episodes; may be persistent, if underlying disease progresses.
- Persistent: Prolonged episode that can be terminated by electrical or chemical cardioversion.
- Permanent: Sinus rhythm cannot be restored.

Slow Pulse Rate [Complete Heart Block (CHB)]

The usual instructions are:

- Examine the pulse.
- Examine the pulse and precordium.

Presentation of a Case

- Pulse: 40/min, high volume, normal rhythm; there is no radiofemoral delay and the condition of the vessel wall is normal.

My diagnosis is **bradycardia.**

Q: What is the most likely **cause** in this case?
A: As follows:

- Complete heart block
- Drugs, such as β-blocker, digoxin, verapamil.

Q: What are the **causes of bradycardia**?
A: As follows:

Causes of **bradycardia:**

- Sinus bradycardia due to any cause.
- Second-degree heart block.
- Complete heart block.
- Nodal rhythm.

Causes of sinus bradycardia

1. Physiological (due to increased vagal tone): Athlete, during sleep.
2. Pathological:
 - Acute inferior myocardial infarction.
 - Myxoedema (due to reduction of sympathetic activity).
 - Hypothermia. Raised intracranial tension (due to inhibitory effect on sympathetic outflow). Obstructive jaundice (due to deposition of bilirubin in conducting system).
 - Drugs (digoxin, β-blockers, amiodarone and verapamil).

Q: What are the **causes** of complete heart block?
A: The commonest causes are:

1. **Acute CHB:**
 - Acute MI (commonly inferior).
2. **Chronic CHB: Idiopathic fibrosis due to:**
 - Progressive fibrosis of distal His–Purkinje system (Lev disease), in elderly.
 - Progressive fibrosis of proximal His–Purkinje system (Lenegre disease), in younger.

Other **causes** of CHB:

- Cardiomyopathy (ischaemic or idiopathic dilated), myocarditis.
- Drugs (digoxin, β-blockers and amiodarone).
- Cardiac surgery (aortic valve replacement, VSD repair and CABG).
- Radiofrequency ablation of AV node.
- Infiltrative disease (sarcoidosis, amyloidosis and haemochromatosis).
- Infection (infective endocarditis, Chagas disease and Lyme disease).
- Collagen disease (SLE and rheumatoid arthritis).
- Congenital complete heart block: Common in children of mother with SLE (due to transplacental transfer of **anti-Ro antibody** or SSA).
- Neuromuscular (Duchenne muscular dystrophy).

Q: What is the **cause** of congenital heart block?
A: Congenital heart block usually occurs, if the mother is suffering from SLE due to the presence of anti-Ro (SSA) antibody, which crosses the placenta and causes congenital heart block.

Q: What are the **signs of complete heart block**?
A: As follows:

- Pulse: Bradycardia, 20–40 beats/min (40 beats/min), high volume, does not increase by exercise or injection atropine.
- BP: High systolic, normal diastolic and high pulse pressure.
- Neck vein: Cannon waves (large 'a' wave) may be present.
- Heart sounds: Variable intensity of first heart sound.
- Murmur: Systolic flow murmur (due to increased stroke volume).

Q: Why is there **variable intensity** of first heart sound and **systolic murmur**?
A: As follows:

- Variable intensity of first heart sound is due to loss of AV synchrony.
- Systolic flow murmur is due to increased stroke volume.

Q: What is the **mechanism** of cannon wave?
A: Due to loss of AV synchrony, when atria contracts against closed tricuspid valve, backward pressure produces cannon wave.

Q: What is the **ECG change** in CHB?
A: Complete dissociation between **P** and QRS. (See ECG on page 105.)

Q: If pulse rate is high, what are the likely **causes** of CHB?

A: As follows:

- Pulse rate is high in congenital complete heart block and does not require treatment.
- If the block occurs more proximally in AV node (narrow complex escape rhythm).



ECG of complete heart block

Q: What are the **presentations** of complete heart block?

A: Dizziness, blackout or sudden loss of consciousness or syncope (Stokes–Adam attack).

Q: How to **treat** complete heart block?

A: If symptomatic, permanent pacemaker should be given. Treatment is based on cause.

Q: What is **Stokes–Adam attack**? What are the **clinical features** and **treatment**?

A: It is the brief attack of syncope or blackout in a patient with complete heart block due to ventricular asystole. Stokes–Adam attack may also occur in Mobitz type II heart block, ventricular tachycardia or fibrillation, sinoatrial disease.

Clinical features:

- Syncope or blackout with or without preceding dizziness.
- During attack patient is unconscious, looks pale and may have convulsion.
- If asystole persists, there may be cyanosis, pulse is absent, incontinence of urine, pupil is fixed and dilated, plantar is extensor.
- Usually consciousness recovers rapidly followed by flushing.

Treatment:

- Permanent pacemaker (even after a single syncopal attack).
- During attack CPR should be done.

Takayasu Disease

The usual instructions are:

- Examine the pulse.
- Examine the pulse and relevant.

Presentation of a Case

(The patient is usually young female)

- All the pulses of upper limbs are absent, but present in lower limbs.
- BP is undetectable in upper limb and normal or high in lower limb (to see BP in lower limb, an 18-cm cuff is required).
- Bruit is present (mention the location).
- No other abnormality in CVS (occasionally evidence of AR are found).
- There may be less development of upper part of the body.

My diagnosis is **Takayasu disease** (pulseless disease or aortic arch syndrome).

Q: What is **Takayasu disease**?

A: It is a chronic, inflammatory, granulomatous panarteritis of unknown cause involving the elastic arteries commonly aorta and its major branches, carotid, ulnar, brachial, radial and axillary. Occasionally, may involve pulmonary artery, rarely abdominal aorta, renal artery resulting in obstruction. F:M ratio is 8:1.

Q: What are the **pathological changes** in Takayasu diseases?

A: Panarteritis, intimal hyperplasia, thickening of media, thickening of adventitia, and later on fibrosis.

Q: What are the **clinical features**? What are the **types**?

A: Common in young female, 25–30 years, more in Asians.

- In acute stage, may present with fever, malaise, weight loss, arthralgia, myalgia and high ESR.
- In chronic case, dizziness, giddiness, headache, syncope, claudication in the upper limb. This may be AR, renal artery stenosis or anginal pain. Hypertension in 32–93%.

Types of Takayasu disease (there are **of four types**):

- Type 1: Involves aortic arch and its major branches.
- Type 2: Involves descending aorta and abdominal aorta.

- Type 3: Involves both type 1 and type 2. This may be complicated by aortic regurgitation.
- Type 4: Involves the pulmonary arteries.

Q: How to **diagnose** Takayasu arteritis?

A: Takayasu arteritis is characterized by at least three of the following criteria:

- Age at onset of disease ≤ 40 years.
- Claudication of extremities.
- Decreased brachial artery pulse.
- BP difference >10 mmHg between left and right arm.
- Bruit over subclavian arteries or aorta.
- Arteriographic abnormality.

Investigations:

- CBC (high ESR and normocytic normochromic anaemia).
- Chest X-ray shows cardiomegaly and widening of aorta.
- Aortography of aortic arch and its branches; renal angiogram shows narrowing, coarctation and aneurysmal dilatation.
- Serum immunoglobulin is high.

Treatment:

- High-dose corticosteroid: Prednisolone 40–60 mg daily or 1–2 mg/kg. If refractory to steroid or difficult to taper steroid, methotrexate up to 25 mg weekly. Cyclophosphamide may be used in resistant case also.
- Reconstructive vascular surgery in selected case. Angioplasty, stenting or bypass surgery may be done, if there is vascular complication.
- Treatment of hypertension.

Prognosis: 95% survive at 15 years.
Complications: Heart failure, stroke.

Coarctation of Aorta

The usual instructions are:

- Examine the pulse.
- Examine the pulse and relevants.
- Examine the pulse and auscultate the heart.

Presentation of a Case

- Pulse: 70/min, normal in rhythm, high volume in upper limb, femoral pulse is very feeble. There is radiofemoral delay.
- BP: 220/110 mmHg in upper limb (and low in lower limb).
- JVP: Normal.
- Carotid pulse: High volume and vigorous.
- There is visible suprasternal, right carotid pulse and supraclavicular pulsation.

On inspection:

- Visible cardiac impulse.
- Visible dilated tortuous artery around the scapula, anterior axilla and over the left sternal border (collateral vessels are best seen by sitting and bending forward, with arm hanging by the side).

On palpation:

- Apex beat: In left ... intercostal space, heaving in nature.
- There may be thrill over the collateral vessels.

On auscultation:

- Heart sounds are normal.
- Systolic murmur audible in ... intercostal space close to the sternum and better heard in fourth intercostal space posteriorly (site of coarctation). May be ejection click, ESM in aortic area and EDM (bicuspid aortic valve or dilatation of aortic valve due to aneurysm causing AR).

My diagnosis is **coarctation of aorta.**

Q: Why is it a case of coarctation of aorta?

A: Because radial pulse is high volume, femoral pulse is feeble and there is radiofemoral delay. Also, the BP is very high in upper limbs and very low in lower limbs.

Q: Why **murmur** in coarctation of aorta?

A: Usually due to increased flow through collateral vessels; also, may be due to associated congenital bicuspid aortic valve.

Q: What are the **types** of coarctation of aorta?

A: There are two types, viz.:

- Postductal (adult type): Commonly below the origin of left subclavian artery, where ductus arteriosus joins the aorta.

- Preductal (infantile type, 2%): Above the origin of left subclavian artery. In such cases, left Left radial pulse is weak and rib is notched on right side. Without other communication, the patient does not survive, and may be associated with PDA.

Q: What are the **sites of collaterals?**

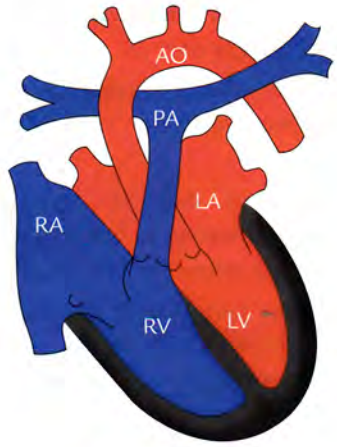
A: Severe narrowing of the aorta encourages the formation of collateral arterial circulation involving the periscapular, internal mammary and intercostal arteries; may result in localized bruit.

Q: What **type** of hypertension develops and why?

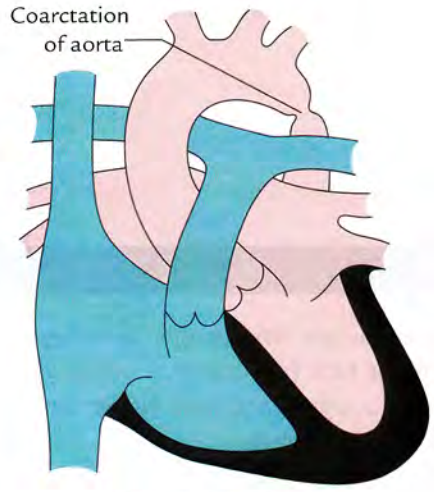
A: Usually systolic hypertension; diastolic may be normal. Causes of hypertension are:

- Mechanical.
- Renin–angiotensin mechanism (due to coarctation, less blood flow to kidney).
- Resetting of baroreceptors.

N.B. Collateral vessels are formed involving periscapular, internal mammary and intercostal arteries.



Normal heart



Coarctation of aorta

Q: What is **reverse coarctation?**

A: When pulse is absent in upper limb, but present in lower limb, it is called reverse coarctation. It occurs in Takayasu disease.

Q: What are the **complications** of coarctation of aorta?

A: As follows:

- Hypertension and its complication (LVF and CVA).
- Infective endocarditis.
- Rupture at the coarctation site.
- Dissecting aneurysm.
- Aneurysm of aorta.
- Subarachnoid haemorrhage (rupture of berry aneurysm of circle of Willis).

Q: What are the **causes of death** in coarctation of aorta?

A: As follows:

- Acute LVF.
- Cerebral haemorrhage.
- Dissecting aneurysm.
- Subarachnoid haemorrhage (due to rupture of aneurysm of circle of Willis).

Q: What are the **associations** in coarctation of aorta?

A: As follows:

- Bicuspid aortic valve (in 50% cases).
- VSD.
- PDA.
- Aneurysm of circle of Willis (5–10% cases).
- In female, Turner syndrome.
- Occasionally, Marfan syndrome.

N.B. Remember the following points:

- Coarctation of aorta is twice more in male than female. M:F ratio is 2:1.
- It is 7% of all congenital heart diseases.
- Even if there is hypertension, renal involvement is unusual and fundal changes are also unusual.

Q: What are the **causes** of coarctation?

A: As follows:

- Congenital (the commonest).
- Rarely, may be acquired in trauma, Takayasu disease.

Q: What are the **presentations** of coarctation of aorta? What **investigations** do you suggest?

Presentations:

- May be asymptomatic.

- Symptoms such as headache, nose bleeding, claudication of lower limbs and cold legs (due to poor blood flow in lower limb).

Investigations:

1. X-ray chest PA view:
 - Poorly developed aortic knuckle (or elongated aortic knuckle), cardiomegaly, poststenotic dilatation of aorta.
 - Rib notching, mostly at the middle part posteriorly, due to enlargement of intercostal arteries from third rib downwards (first and second ribs are not affected because intercostal arteries here arise from subclavian artery above the constriction).
 - Figure of **three** (constriction at coarctation, prestenotic and poststenotic dilatation).
2. ECG (LVH).
3. Others: CT scan and CMR angiography are ideal for confirming the diagnosis. Echocardiogram and aortography may also be done.

Q: What are the causes of **unilateral rib notching**?
A: As follows:

- Coarctation of aorta (before the origin of left subclavian artery).
- Blalock–Taussig shunt (iatrogenic, done in Fallot tetralogy).
- Subclavian artery obstruction.
- Neurofibromatosis.
- Congenital.

Q: What are the causes of **bilateral rib notching**?
A: Usual causes are:

- Coarctation of aorta (after the origin of left subclavian artery).
- Neurofibromatosis.
- Congenital.

Q: What is the **treatment** of coarctation of aorta?
A: As follows:

- Coarctation of aorta should be treated surgically as early as possible, preferably before 5 years of age. Surgical resection and end-to-end anastomosis is usually done. If coarctation is extensive, then prosthetic vascular graft may be done. (If surgery is done during adolescence or adulthood, hypertension may persist in up to 70% cases because of irreversible changes in arterioles or renal damage. If done in early childhood, hypertension usually resolves completely.)
- Balloon angioplasty may be helpful. It is particularly effective after restenosis.

Prognosis after surgery:

- Surgical correction in childhood gives a good 25 year survival in 83%. If surgery is delayed until adulthood, 25 year survival rate drops to 75%. Without surgery, only 25% live up to 50 years of age, while cardiac failure occurs in two-third of surviving patients over 40.
- In few cases, there is restenosis as the child grows. This can be treated by balloon angioplasty.
- If operation is delayed, patient may have persistent hypertension because of irreversible changes in the arterioles.
- May develop paradoxical hypertension due to baroreceptor-induced increased sympathetic activity (detected by increased serum and urinary catecholamines).
- Coexistent bicuspid aortic valve, which occurs in over 50% of cases, may lead to progressive AS or regurgitation and also requires long-term follow-up.

Marfan Syndrome

The usual instructions are:

- Look at the patient and do the relevants.
- Examine the heart and relevants.

Proceed as follows:

- Look at the patient carefully (patient looks tall, lean and thin).
- Measure height from pubis to vertex and pubis to sole of foot (pubis:sole > pubis:vertex), lower segment > upper segment, height and arm span (arm span > height).
- Look at the palate, eyes, any bony deformity and hyperextensibility of joints.
- Finally examine the heart.

Presentation of a Case

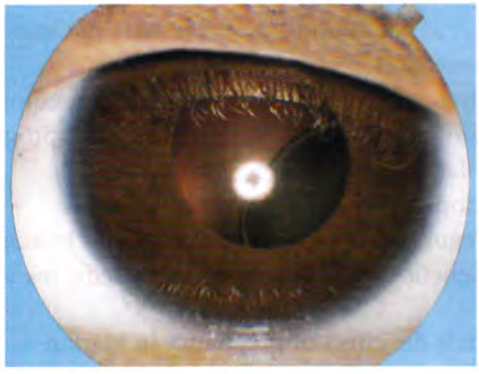
- The patient is tall, lean and thin. Face is long and narrow.
- Long upper and lower limbs. There is arachnodactyly (long, thin, spider fingers and toes). Hyperextensibility of joints. Arm span > height (mention the exact measurement in centimetre or inch). Lower segment > upper segment (mention the exact measurement in centimetre or inch).
- Eyes with blue sclera, subluxation of lens (ectopia lentis usually upward and outward, iridodonesis, atrophy of iris).
- Palate is high arched.
- Chest is pectus excavatum, carinatum and kyphoscoliosis.
- Heart evidences of AR or MR.



Arachnodactyly (hand)



Arachnodactyly (fingers and toes)



Dislocation of lens



High arch palate

My diagnosis is **Marfan syndrome.**

Q: What are the associations in Marfan syndrome?

A: As follows:

- Cystic disease in lung may cause spontaneous pneumothorax (may be recurrent), bullae, apical fibrosis, aspergilloma and bronchiectasis.
- Inguinal or femoral hernia and decreased subcutaneous fat.
- Small nodule or papule in skin of neck (Miescher elastoma).

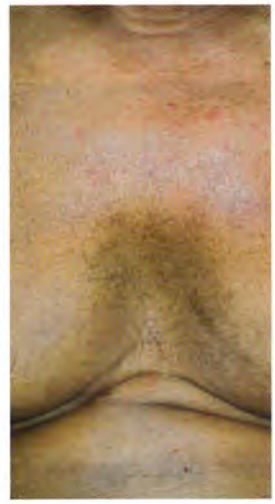
Q: What is Marfan syndrome?

A: It is a connective tissue disorder inherited as autosomal dominant (AD) trait due to mutation in the fibrillin-1 gene—a component of extracellular matrix. The fibrillin gene is located in the long arm of chromosome 15 (15q21.1). Marfan syndrome is characterised by triad of eye, skeletal and cardiac abnormalities.

1. **Eye:**
 - Blue sclera.
 - Subluxation or dislocation of lens (ectopia lentis).
 - Iridodonesis (tremor of iris).
 - Heterochromia iris (various colour of iris).
 - Myopia.
 - Retinal detachment.
 - Glaucoma.
2. **Skeletal:**
 - Tall, lean and thin, arachnodactyly. Hyperextensibility of joints.
 - High arch palate.

- Kyphosis or scoliosis. High pedal arch or pes planus.
- Pectus excavatum or carinatum or asymmetry of chest.

3. CVS:
 - AR (due to aortic root dilatation, secondary to cystic medial necrosis involving aorta).
 - MR (with mitral valve prolapse).



Pectus excavatum



N.B. Marfan syndrome may cause dissecting aneurysm, infective endocarditis may be associated with coarctation of aorta.

Diagnosis of Marfan syndrome is made if:

- Positive family history and features of two different systems.
- There are features in three different systems.

Causes of death in Marfan syndrome:

- Dissecting aneurysm.
- Heart failure.

Q: What **investigation** should be done in Marfan syndrome?

A: As follows:

- X-ray chest (may be normal, may show features of aortic aneurysm, and unfolding or widened mediastinum. Pneumothorax or scoliosis may be present).
- ECG (to see any arrhythmia).
- Echocardiogram (mitral valve prolapse, aortic regurgitation, MR, aortic root dilatation).
- CT or CMR (to see aortic dilatation).

Q: How to **treat** Marfan syndrome?

A: As follows:

- β-blocker (propranolol) reduces aortic dilatation and prevents the risk of aortic rupture or dissecting aneurysm.
- ACE receptor blocker: In Marfan syndrome there is upregulation of TNF-β, which is specifically inhibited by ACE blocker. It prevents aortic root dilatation.
- Avoid strenuous exercise to prevent aortic dissection.
- Surgery: Elective replacement of ascending aorta and aortic valve in patient with progressive dilatation of aorta (>5 cm).
- Prophylaxis for infective endocarditis.
- Regular checkup (echocardiography) annually.
- Genetic counselling and orthopaedic measures.

Q: What is the **effect of pregnancy** in Marfan syndrome?

A: Pregnancy is well tolerated, if there is no serious cardiac problem. It is avoided, if aortic root dilatation is >4 cm with AR. Maternal death may occur due to aortic dissection during pregnancy. Early premature abortion may also occur. Echocardiogram should be done every 6–8 weeks throughout pregnancy and 6 month postpartum. BP should be regularly monitored. Vaginal delivery is possible; Caesarean section is not done routinely. If aortic root is >4.5 cm delivery should be done at 39 weeks by induction or Caesarean section. β-blocker should be continued throughout pregnancy.

Q: What is your **differential diagnosis** and how to differentiate?

A: Homocystinuria (due to deficiency of enzyme cystathionine synthetase).

	Features	Homocystinuria	Marfan syndrome
1.	Inheritance	AR	AD
2.	Lens	Dislocated downward	Dislocated upward
3.	Skeletal abnormality	Osteoporosis—common.	Osteoporosis—less common, but flat foot, scoliosis, pectus excavatum are common
4.	Aortic regurgitation	Rare	Common
5.	Mental retardation	Common	No
6.	Vascular complication	Prone to develop thrombosis	No
7.	Life expectancy	Reduced from cardiovascular risk	May be normal
8.	Test (urine)	Cyanide nitroprusside (positive)	Cyanide nitroprusside (negative)
9.	Spectroscopic examination (urine)	Homocystine detected	No
10.	Pyridoxine	May respond	No

Dextrocardia

Usual instructions:

- Examine the precordium.

Presentation of the Case

- Apex beat is absent on left side, but present on right side, in... intercostal space,... cm from midline.
- Heart sounds are less heard in left side, but better heard in right side of chest.

My diagnosis is **dextrocardia.**

Q: What is **dextrocardia**?
A: When heart is on the right side of chest, but other visceras remain on their usual sites, it is called dextrocardia.

Q: What is **situs inversus**?
A: Dextrocardia with reversal of sites of other visceras (stomach on right side, liver on left side, right lung is on the left side, left lung is on the right side and the appendix on the left side).

Q: What is **levocardia**?
A: When heart is on left side, but there is reversal of the site of other visceras, it is called levocardia (stomach on right side, liver on the left side, right lung is on the left side and left lung is on the right side).

Q: What is **mesocardia**?
A: When cardiac apex is in the midline, it is called mesocardia.

Q: If the patient has dextrocardia, what **else** do you want to see?
A: Lung base for crepitations and clubbing (bronchiectasis), and associated with Kartagener syndrome. Also need to see liver for situs inversus.

Q: Suppose a patient has dextrocardia. Suggest **one investigation**.
A: PNS X-ray (to see frontal sinusitis or agenesis in Kartagener syndrome).

Q: What is **Kartagener syndrome**?
A: It is characterised by:
- Dextrocardia.
- Bronchiectasis.
- Frontal sinusitis or frontal sinus agenesis.
- Other features include situs inversus, infertility, otitis media, and ciliary immotility.

Q: What is the **prognosis** in situs inversus?
A: Usually normal lifespan.

Q: What is the clinical **importance** in situs inversus?
A: As follows:
- Diagnosis of appendicitis may be missed (it is on the left side).
- Liver disease may be missed and liver biopsy may be mistakenly done on right side.

N.B. Dextrocardia may occur in Turner syndrome.

Pericardial Effusion

Usual instructions:

- Examine the CVS.

Presentation of a Case

- Pulse: 110/min (tachycardia), low volume, there may be pulsus paradoxus (indicates cardiac tamponade).
- JVP: Raised, Kussmaul sign positive (raised JVP during inspiration).
- BP: Low systolic, normal diastolic and narrow pulse pressure.

On inspection:

- Nothing significant.

On palpation:

- Apex beat: Difficult to palpate (or could not be palpated).

On percussion:

- Area of cardiac dullness is increased.

On auscultation:

- Heart sounds are muffled (or distant).
- Bronchial sound at the left inferior angle of scapula (Ewart sign, which is due to the compression of the base of the left lung due to enlarged heart).

My diagnosis is **pericardial effusion.**

Q: How to **confirm** your diagnosis?

A: By echocardiogram (it shows **echo-free** zone). Pericardiocentesis is definitive.

Q: If echocardiogram is not available, how to diagnose pericardial effusion?

A: Chest X-ray in a Trendelenburg position (base of heart will be wide).

Q: What are the **ECG findings** in pericardial effusion?

A: Low-voltage tracing and sinus tachycardia.

Q: What are the **causes** of pericardial effusion?

A: As follows:

- Following acute infective pericarditis (bacterial and viral).
- TB.
- Collagen diseases (SLE and rheumatoid arthritis).
- Cardiac causes (post-MI, postcardiotomy and Dressler syndrome).
- Myxoedema.
- Lymphoma.
- Neoplasm (secondary from carcinoma of breast and bronchial carcinoma).
- Uraemia and dialysis.
- Trauma.
- Aortic dissection.
- Drugs (practolol, phenylbutazone, procainamide and hydralazine).
- After radiotherapy.

Q: What **investigations** are done in pericardial effusion?

A: As follows:

1. Chest X-ray (PA view shows heart is enlarged in TD, globular, pear shaped with clear margin and lung fields are oligaemic).
2. Full blood count (ESR high in TB and SLE).
3. ECG (low-voltage tracing and tachycardia).
4. Echocardiogram, the colour Doppler may show increased flow through tricuspid and pulmonary valve, decreased flow through mitral valve during inspiration.
5. Pericardiocentesis, see the physical character, analysis of pericardial fluid to find out the cause (Gram staining, cytology, biochemistry, culture and sensitivity, AFB and malignant cell). Pericardial biopsy may be needed sometimes.
6. MRI (very helpful to see haemopericardium or loculated pericardial effusion).
7. Other investigations according to suspicion of causes:
 - TB (MT, sputum for AFB).
 - Collagen disease (RA test, ANA, anti-double strand DNA).
 - Hypothyroidism (FT_3, FT_4 and TSH).

Q: How to **confirm** a case of tuberculous pericardial effusion?

A: Isolation of organism from pericardial fluid by:

- AFB staining (positive in 25% cases);
- Culture (Löwenstein–Jensen media);
- PCR.

Q: How to **treat** pericardial effusion?

A: The commonest cause is TB. Hence, antituberculous drug plus prednisolone should be given. Other treatment is needed according to primary cause (e.g. SLE). Surgical drainage may be necessary, especially if viscus loculated or recurrent effusion.



Pericardial effusion

Q: What are the causes of **recurrent pericardial effusion?**

A: Mostly due to malignancy, may be in uraemia. In such case, pericardial fenestration (creation of window in the pericardium) is done to allow slow release of fluid in the surrounding tissue. Surgical drainage or partial pericardiectomy may also be necessary.

Q: How **pericardiocentesis** is done? What are the complications of paracentesis?

A: It is better done under ultrasonographical or echocardiographical guidance. Aspiration needle is introduced through left costoxiphoid junction, directed upward, backward and towards the left shoulder. Needle may also be introduced lateral to the apex beat.

Q: What are the **complications** of paracentesis?

A: As follows:

- Injury to coronary artery and ventricles.
- Dysrhythmia.
- Bleeding (which may aggravate cardiac tamponade).

Q: What is **cardiac tamponade?**

A: It is a state of compression of heart in rapidly developing pericardial effusion, which interferes with diastolic filling of heart and the patient develops features of shock. If there is rapid accumulation, even 200 mL of fluid can cause cardiac tamponade. However, if slow accumulation of fluid occurs, 2000 mL may be required for cardiac tamponade.

Q: What are the **causes** of cardiac tamponade? What are the features of cardiac tamponade? How to **treat?**

A: As follows:

- Trauma or cardiac surgery (causing haemopericardium).
- Malignancy (repeated effusion may occur).
- Myocardial rupture.
- Dissecting aortic aneurysm.
- Sometimes, any cause of pericardial effusion can cause.

Clinical features:

- Heaviness and compression in chest.
- Dyspnoea.
- Features of shock.

Signs of cardiac tamponade (see signs of pericardial effusion).

Treatment:

- It is a medical emergency. Pericardiocentesis should be done.
- Treatment of primary cause.

Chronic Constrictive Pericarditis

Usual instructions:

- Examine the CVS.

Presentation of a Case

- Pulse: 120/min (tachycardia), low volume. Pulsus paradoxus may be present.
- JVP: Raised.
- BP: 100/70 mmHg.
- Kussmaul sign positive (raised JVP on inspiration).
- Fall of Y descent (Friedrich sign).

On inspection:

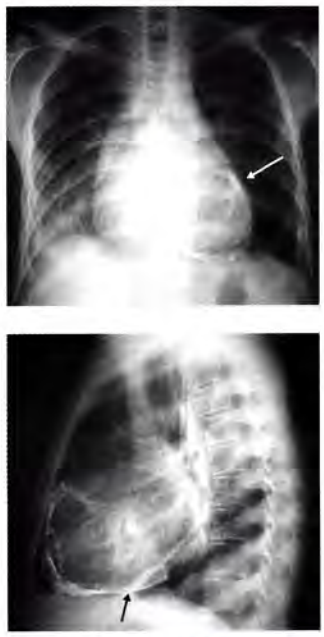
- Nothing significant.

On palpation:

- Apex beat: Palpable (in the left ... intercostal space, ... cm from the midline).

On auscultation:

- Pericardial knock (a third heart sound, due to rapid ventricular filling).



Pericardial calcification

My diagnosis is **chronic constrictive pericarditis.**

Q: What **other signs or relevant** do you like to look for?

A: Ascites (early feature), oedema (late feature) and hepatomegaly.

Q: What is **chronic constrictive pericarditis?**

A: It is a disorder characterised by progressive thickening, fibrosis and calcification of pericardium. Commonly, involves right side of the heart.

Q: What are the **presentations and signs** of chronic constrictive pericarditis?

A: Most features are due to systemic venous congestion. Symptoms are:

- Cough, breathlessness on exertion, may be orthopnoea, paroxysmal nocturnal dyspnoea.
- Weakness, dizziness, giddiness, anorexia, nausea and vomiting.
- Abdominal swelling, later ankle swelling.

Signs are:

- Tachycardia, low-volume pulse.
- Pulsus paradoxus may be present.
- JVP: Raised, fall of Y descent (Friedrich sign). Kussmaul sign positive (raised JVP on inspiration).
- Pericardial knock (a third heart sound due to rapid ventricular filling).
- Enlarged tender liver.
- Ascites.
- Peripheral oedema later on.

Q: What are the **causes** of chronic constrictive pericarditis?

A: As follows:

- Any cause of calcification of pericardium can cause chronic constrictive pericarditis.
- Infection (TB and coxsackie B infection).
- Haemopericardium (which may be due to trauma, myocardial rupture after infarction and dissecting aneurysm).
- Collagen disease (rheumatoid arthritis).
- Cardiac operation.
- Mediastinal irradiation.
- Fungal infection (histoplasmosis).
- Rarely, after acute purulent pericarditis.
- Idiopathic.

N.B. Calcification commonly involves right side of the heart and can be seen by fluoroscopy. Calcification does not always means constriction. RF does not causes chronic constrictive pericarditis.

Q: What are the **complications** of chronic constrictive pericarditis?

A: As follows:

- Atrial fibrillation (in 30% cases).
- Ascites.
- Myocardial fibrosis.

Q: What **investigations** are done?

A: As follows:

1. Chest X-ray (PA and lateral view): Relatively small heart, pericardial calcification in 50% cases.
2. ECG (low-voltage tracing, tachycardia, and T inversion).
3. Echocardiogram (thick calcified pericardium, small ventricular cavities with normal wall thickness, large atrium, dilatation of inferior vena cava, abnormal septal motion and immobile heart).
4. Colour Doppler (reduction of flow along mitral valve and pulmonary vein during inspiration. Opposite occurs during expiration).
5. CT scan or CMR.
6. Cardiac catheterisation shows that diastolic pressure is equal in all chambers (left and right ventricles), end-diastolic pressure (EDP) is equal in left and right atrium.
7. Other investigations (according to suspicion of cause).
8. Endomyocardial biopsy: May be necessary to differentiate from restrictive cardiomyopathy in difficult cases.

Q: How to **treat** chronic constrictive pericarditis?

A: As follows:

- Surgery: Complete resection of pericardium (helpful in 50% cases).
- If TB is present, early pericardiectomy with anti-TB drug should be given. If no calcification, anti-TB drug should be given first. If the haemodynamic status of the patient remains static or deteriorates after 4–6 weeks, pericardiectomy should be done.

- Treatment of primary cause should be done.
- After surgery, persistent constriction and myocardial fibrosis may be present. AF may occur after full recovery.

Q: What are the **differential diagnoses** of chronic constrictive pericarditis?

A: As follows:

- Restrictive cardiomyopathy.
- CCF.

Q: How to differentiate chronic constrictive pericarditis from CCF?

A: As follows:

Features	CCF	Chronic constrictive pericarditis
1. Breathlessness	Common, more on exertion	Not common in rest, marked only on exertion
2. Pulsus paradoxus	No	May be present
3. JVP	Raised, but no Kussmaul sign	Raised, Kussmaul sign positive, may be Y descent
4. Cardiomegaly	Present	Absent
5. Oedema	Early feature than ascites	Ascites early, oedema late feature
6. On auscultation	Murmur may be present	Pericardial knock is present

Q: How to **differentiate** chronic constrictive pericarditis from restrictive cardiomyopathy?

A: As follows:

Features	Chronic constrictive pericarditis	Restrictive cardiomyopathy
1. Apex beat	Not felt	Well felt
2. Heart	Normal and pericardial knock is present	May be enlarged, LVH and LVF may be present
3. ECG	Low-voltage tracing, tachycardia	Bundle branch block, Q-wave may be present
4. Echocardiogram	Changes in pericardium	Myocardium is thick
5. Colour Doppler	Respiratory variation in A:V flow	No change
6. CT or CMR	Pericardium is thick with calcification	Thick ventricle

Acute Pericarditis

Usual instructions:

- Examine the CVS.

Presentation of a Case

- Pulse: 80/min, normal in volume and character.
- JVP: Not raised.
- BP: 120/75 mmHg.

On inspection:

- Nothing significant.

On palpation:

- Apex beat: Palpable (in the left … intercostal space, …cm from the midline).

On auscultation:

- Heart sounds are normal.
- There is pericardial rub in left third and fourth intercostal spaces near the left lower parasternal border.

My diagnosis is **acute pericarditis**.

Q: What are the **ECG findings** in acute pericarditis?

A: As follows (see the ECG on the right):

ST is elevated with upward concavity (chair shaped or saddle shaped) that is better seen in L_I, L_{II}, aVL, aVF, V_4 to V_6.

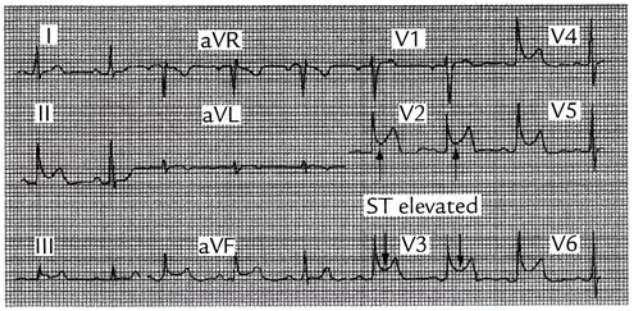
T may be upright in acute phase.

Q: How to **differentiate** acute pericarditis from acute MI by ECG?

A: As follows:

In MI, there is ST elevation with upward convexity.

In pericarditis, there is ST elevation with upward concavity. (Pericardium envelops the heart; hence, ST changes are more generalised and seen in most leads.)



ST elevation in II, aVF, V_2 to V_6

Q: What is the **clinical finding** in acute pericarditis?

A: Pericardial rub. It is a high-pitched, harsh, scratching, grating, leathery sound, to-and-fro in quality. Better heard over the left lower parasternal area with the patient leaning forward (bare area of heart; it is the part of heart that is not covered by lung). It is usually heard in systole, but may be present in diastole, augmented by pressing the stethoscope and is present after holding the breath (to differentiate from pleural rub).

Q: What are the **presentations** of acute pericarditis?

A: Chest pain, which is retrosternal. It is usually sharp or stabbing in nature, may radiate to the shoulder and neck, aggravated by movement, lying down, deep breathing, exercise and swallowing. This may be relieved by sitting or bending forward.

Q: What are the **causes** of acute pericarditis?

A: As follows:

- Following acute myocardial infarction (usually in second or third day) or Dressler syndrome (later).
- Viral (Coxsackie B, echovirus, also HIV): Common cause.
- Bacterial (*Staphylococcus aureus, Streptococcus, Pneumococcus, Haemophilus influenzae*).
- Tuberculous pericarditis.
- Fungal (histoplasmosis, coccidioidomycosis).
- Rheumatic fever.
- Uraemia (an indication of urgent dialysis).
- Malignancy (from carcinoma of bronchus, breast, lymphoma, leukaemia), rarely primary tumour of heart (mesothelioma).
- Myxoedematous pericarditis.
- Drugs (doxorubicin, cyclophosphamide).
- Collagen disease (SLE, scleroderma).
- Others: Postradiation, postsurgical, idiopathic.

Q: What are the **commonest causes** of acute pericarditis?

A: Viral infection and myocardial infarction.

Q: What are the features of **pericarditis** after myocardial infarction?

A: Pericarditis occurs in 20% of patient in the first few days following myocardial infarction, more commonly anterior and ST elevation myocardial infarction with high serum cardiac enzymes. Incidence is less (5–6%) with thrombolysis. Pericarditis may occur as Dressler syndrome, 2–10 weeks after infarction.

Q: How would you **treat** acute pericarditis?

A: As follows:

- To relieve pain: NSAIDs (indomethacin or ibuprofen or aspirin) is given.
- In severe or recurrent case, corticosteroid should be given.
- If no response to steroid, azathioprine or colchicine may be given.
- If recurrence with no response to medical treatment, pericardiotomy may be done.
- Treatment of primary cause should be done. Antibiotic, if bacterial infection. Anti-Koch, if TB is suspected. Other treatment according to cause.

N.B. 20% cases of acute pericarditis may develop idiopathic relapsing pericarditis. Treatment is as above. If pericarditis persists 6–12 months following acute attack, it is considered chronic.

Rheumatic Fever

The usual instructions are:

- Examine the knee joints (or other joints).
- Examine the upper limbs or lower limbs. What are your findings? What would you like to see in the heart?

Presentation of a Case

(Supposing both knee and elbow joints)

- Both the **knee** and **elbow** joints are swollen.
- Skin is red and shiny.
- Local temperature is raised and the joints are very tender.
- There is restricted movement of the joints (because of pain).

My differential diagnoses are:

- RF (if deformity is present, it is **against** RF).
- Reactive arthritis or Reiter syndrome.
- Juvenile idiopathic arthritis (JIA or JCA).
- Seronegative arthritis (ankylosing spondylitis and enteropathic arthritis).
- Rheumatoid arthritis.
- Psoriatic arthritis (if any skin lesion, nail change).
- Acute gouty arthritis.
- Septic arthritis.
- Traumatic arthropathy.

Q: What is the **likely diagnosis** in this case?

A: Rheumatic fever.

Q: What **relevants** do you like to examine in RF?

A: As follows:

- I would like to examine the heart to see evidence of carditis (pericarditis, myocarditis, and endocarditis).
- Erythema marginatum (pinkish rash with slightly raised margin, mostly over the trunk and limbs).
- Subcutaneous nodules (found over bony prominences, joints and tendons. These are small and painless and are found over the extensor surface).
- Rheumatic chorea.

Q: What are the **presenting complaints** of a patient with RF?

A: RF usually occurs in children and young adults.

Features are:

- Migrating (fleeting), nondeforming polyarthritis involving the large joints (knee, ankle and elbow) and wrists with fever, may be continuous, high grade is the presenting feature in 75% cases.
- Palpitation and chest pain (due to carditis in 50% cases).
- Skin rash (erythema marginatum), subcutaneous nodules.
- Involuntary movement (chorea in 10–30% cases).
- Malaise, weakness and fatigue.

Q: What **investigations** will you do in RF?

A: As follows:

1. Hb, TC, DC, ESR (high ESR and leucocytosis).
2. C-reactive protein [(CRP) high].
3. Antistreptolysin O (ASO titre)—may be high, in adult >200, in children >300).
4. Throat swab culture (to find *Streptococcus haemolyticus*).
5. Chest X-ray (cardiomegaly, pulmonary oedema may be present).
6. ECG.
7. Echocardiography (to see valve abnormality and cardiomegaly).
8. RA factor (to exclude RA) and ANA (to exclude SLE), if needed.

Q: What is **RF? What is the mechanism or pathogenesis** of RF?

A: It is a multisystem disorder, occurs as a sequela to pharyngitis by *Streptococcus β-haemolyticus* group A. It is due to autoimmune reaction between the antigen (M protein) of *Streptococcus haemolyticus*, and cardiac myosin and sarcolemmal membrane protein (laminin). As a result, antibody is produced against streptococcal enzyme, causing inflammation in the endocardium, myocardium and pericardium as well as joints and skin. There is formation of 'Aschoff nodule' in heart only.

Q: What is **Aschoff nodule?**

A: It is a granulomatous nodule composed of central fibrinoid necrosis and multinucleated giant cells, surrounded by macrophage and T-lymphocytes. It occurs throughout the heart. It is pathognomonic of RF.

Q: Which **joints** are commonly involved in ARF?

A: Commonly large joints, ankle, wrist, knee and elbow (usually does not involve small joints of the hands and feet, rarely involves hip joint).

Q: What are the **diagnostic criteria** of RF?

A: It is diagnosed by revised 'Jones criteria'. Following an attack of *Streptococcus pharyngitis*, there is usually a latent period of 1–3 weeks.

1. **Major criteria:**
 - Carditis.
 - Shifting polyarthritis.
 - Rheumatic chorea.
 - Erythema marginatum.
 - Subcutaneous nodule.
2. **Minor criteria:**
 - Fever.
 - Arthralgia.
 - Previous history of RF.
 - High ESR or CRP.
 - Leucocytosis.
 - First- or second-degree AV block in ECG.

All of the **above** along with supportive evidence of previous streptococcal infection, such as recent scarlet fever, raised ASO or other streptococcal antibody titre (anti-DNAse or antihyaluronidase) and positive throat culture are seen.

Diagnosis is done by two or more major criteria, or one major and two or more minor criteria plus supportive evidence of streptococcal infection.

Q: What are the **signs of carditis?**

A: RF can cause carditis involving all the layers of the heart (endocardium, myocardium and pericardium) called pancarditis.

Signs of endocarditis:

- Heart sounds are soft.
- PSM (due to MR).
- Mid-diastolic murmur [MDM (Carey Coombs murmur)].
- EDM (due to AR).

Signs of myocarditis:

- Tachycardia: Soft heart sound, S3 gallop.
- Cardiomegaly: Features of heart failure.

Signs of pericarditis:

- Pericardial rub (pericardial effusion may occur).

Q: What is **erythema marginatum**?

A: It is characterised by transient raised pink or red rash, blanches on pressure, with clear centre and round margin. It occurs in 10% of cases, found mostly on the trunks and proximal limbs (but not on face). It may coalesce into crescent- or ring-shaped patch.

Q: What is **subcutaneous nodule**?

A: These are small, firm and painless pea-shaped nodules, felt over bony prominence and tendons or joints in extensor surface, present in 10–15% cases.

Q: What is **Sydenham chorea** (St. Vitus' dance)?

A: It is a neurological manifestation of acute RF, usually occurs after 3 months of an acute attack, when almost all other signs disappear.

- It occurs in one-third of cases, common in child and adolescent, more in female of 5–15 years of age.
- Associated with emotional instability, irritability, inattentiveness and confusion. It may occur without any features of acute RF. Carditis is common, may be the first manifestation.
- Speech may be explosive and halting.
- ESR, ASO titre and CRP are usually normal.
- Rheumatic chorea is usually self-limiting and recovers within few months.
- Relapse may occur only in few cases, occasionally during pregnancy (chorea gravidarum) or in those who use oral contraceptive pill.
- Treatment needs sedation along with other treatment and prophylaxis of RF.
- 25% of cases develop chronic rheumatic heart disease in course of time.

Q: How to **treat** acute RF?

A: As follows:

1. Complete bed rest (until disease activity resolves).
2. Oral phenoxymethyl penicillin 250 mg 6 hourly for 10 days or single injection of benzathine penicillin 1.2 million units, deep IM in the buttock (to eliminate the streptococcal infection). Erythromycin may be given if allergic to penicillin.
3. Analgesic (to relieve pain): Aspirin 60 mg/kg per day in divided doses. Higher dose may be needed.
4. Other treatment for symptomatic relief of cardiac failure, pericarditis and others:
 - For carditis or severe arthritis: Corticosteroid may be given (prednisolone 1–2 mg/kg daily).
 - For chorea: Diazepam for mild case and haloperidol in severe case may be given.
 - For erythema marginatum and subcutaneous nodules: No treatment is necessary.

Q: What is the **prophylactic** treatment of RF? **How long** it should be continued?

A: Recurrence is common in patients who had carditis during initial episode. In children, 20% recurrence occurs within 5 years. Recurrence is uncommon after 5 years and in patients over 25 years of age.

To prevent recurrence:

- Oral phenoxymethyl penicillin 250 mg 12 hourly or injection benzathine penicillin 1.2 million units deep IM monthly should be given.
- In penicillin-sensitive patients, erythromycin (250 mg 12 hourly) or sulphadiazine (1 g daily) may be used.
- Prophylactic drug should be continued up to 21 years of age or 5 years after the last attack (recurrence after 5 years is rare), whichever is longer.
- It should be extended if an attack has occurred in the last 5 years, if the patient lives in area of high prevalence or has a high exposure to streptococcal infection.
- If there is residual heart disease: Prophylactic should be continued for 10 or 40 years of age, whichever is longer.

Q: What are the **signs of activity** in RF?

A: Persistent fever, tachycardia, high ESR, leucocytosis and evidence of carditis.

N.B. Remember the following points:

- Skin infection with streptococci is not associated with RF.
- Streptococcal sore throat may not be present in some cases.
- Rheumatic fever licks the joints and kills the heart.
- More than 50% patients of RF with carditis will develop chronic valvular disease after usually 10–20 years.
- All the cardiac valves may be involved as a sequela of complication of RF called chronic rheumatic heart disease. It commonly affects the mitral valve (70%), aortic valve (40%). Rarely, involves tricuspid (10%) and pulmonary (2%) valves.
- In chronic rheumatic heart disease, there is no history of RF in 50–60% cases.

Q: What are the **causes of migrating** polyarthritis?

A: Rheumatic fever, septicaemia, gonococcal arthritis, syphilitic arthritis, lyme arthritis, hyperlipidaemia (type II), SLE, sarcoidosis, bacterial endocarditis, Whipple disease.



Effusion in right knee in rheumatic fever



Swelling of knee joint in rheumatic fever

Hypertrophic Cardiomyopathy

Instruction by the examiner:

- Examine the CVS.

Presentation of a Case

1. Pulse: 88/min, normal volume, normal in rhythm, no radiofemoral or radio-radial delay.
2. Carotid pulse: Jerky.
3. JVP: Normal ('a' wave may be prominent).
4. BP: 95/80 mmHg (low systolic, normal diastolic and narrow pulse pressure).
5. Precordium shows:
 - Apex beat is in the left ... intercostal space ... cm from midline, heaving in nature (may be double apical impulse).
 - A systolic thrill is palpable at apex (or the lower left sternal border).
 - First and second heart sound: Normal in all the areas.
 - Fourth heart sound may be present (due to atrial contraction).
 - There is a harsh ejection systolic murmur at the left lower sternal border.
 - There is a PSM at the apex.

My **differential diagnoses** are:

- MR.
- AS.
- HCM.

Q: What is the more **likely** diagnosis? Why?

A: HCM because of double apical impulse and jerky pulse.

Q: What are the factors that alter the **intensity** of the murmur at left lower sterna border?

A: It increases during standing and valsalva manoeuvre, and decreases during squatting or sustained hand grip.

Q: Why did you find murmur of MR?

A: MR may be associated with HCM.

Q: Why not AS?

A: In AS, the findings are:

- Pulse is low volume and slow rising.
- BP shows low systolic, normal diastolic and narrow pulse pressure.
- Systolic thrill in aortic area.
- Second heart sound shows soft A2 in all the areas, P2 is normal, may be reversed splitting of second heart sound.
- There is a harsh ejection systolic murmur in aortic area and radiates towards the neck.

Q: What **investigations** should be done in HCM?

A: As follows:

- X-ray chest (may be normal).
- ECG: May show LVH, left axis deviation, infarction pattern (Q-wave in inferior and lateral chest lead), deep T inversion (confused with subendocardial myocardial infarction), atrial fibrillation, also bizarre pattern.
- Echocardiogram (diagnostic): Typically shows asymmetric septal hypertrophy, systolic anterior motion (SAM) of mitral valve. May also show MR and small LV cavity.
- Cardiac MR.
- Genetic analysis.

Q: What is **cardiomyopathy**? What are the **types**?

A: Cardiomyopathies are a group of disease that primarily affect the heart muscle and are not due to the result of congenital, acquired valvular, hypertension, coronary arterial or pericardial abnormalities.

It is of three types:

- Dilated cardiomyopathy (ischaemic).
- HCM.
- Restrictive cardiomyopathy.

Q: What is **hypertrophic cardiomyopathy** (HCM)?

A: Hypertrophic cardiomyopathy (HCM) is a disease of the heart muscle characterized by hypertrophy of cardiac muscle with misalignment of the cardiac fibres. Hypertrophy may be generalized or localized to the interventricular septum (asymmetrical septal hypertrophy) or other regions (apical HCM).

N.B. Remember the following points:

- It is a common type of cardiomyopathy. Prevalence is 1:500 to 1:1000, inherited as AD, but may be sporadic in 50% case.
- About half of the patients have a positive family history. First-degree relatives should be screened.
- Previously, it was called hypertrophic obstructive cardiomyopathy (HOCM), but left ventricular outflow obstruction is found only in one-third patients.

Q: What are the **types of HCM**?

A: As follows:

- Asymmetrical septal hypertrophy (70%).
- Basal septal hypertrophy (15–20%).
- Concentric (8–10%).
- Apical/lateral wall (<2%).

Q: What are the **presentations** of HCM?

A: Patient may be asymptomatic. Other features are:

- Angina on effort.
- Dyspnoea on effort.
- Presyncope or syncope on effort.
- Sudden death.

Q: What are the complications of HCM?

A: As follows:

- Sudden death.
- Atrial fibrillation.
- Infective endocarditis.
- Systemic embolism.

Q: How to **treat** HCM?

A: As follows:

1. **Specific measures:**
 - β-blocker, rate-limiting calcium channel blocker (verapamil, diltiazem), and disopyramide for symptomatic relief and prevention of syncope.
 - Amiodarone may be helpful to prevent arrhythmia.
 - In some patients with significant left ventricular outflow obstruction and symptoms, dual chamber pacing may be needed.
 - Outflow tract obstruction can be improved by partial surgical resection (myectomy) or by iatrogenic infarction of the basal septum (septal ablation) by a catheter-delivered alcohol solution.
 - Implantable cardioverter-defibrillator (ICD) should be considered in patient with clinical risk factors for sudden death.
 - Cardiac transplantation may be needed in CHF not responding to treatment.
 - Infective endocarditis prophylaxis may be needed.
2. **Advice:**
 - Vigorous exercise and dehydration should be avoided.
 - Genetic counselling of patients and relatives is essential.

Q: What are the **risk factors** for sudden death in HCM?

A: As follows:

- A history of previous cardiac arrest or sustained VT.
- Recurrent syncope.
- An adverse genotype and/or family history of sudden cardiac death (SCD) (<50 years old).
- Failure of BP to rise during exercise (no change or hypotension).
- Nonsustained VT on 24-h Holter monitoring.
- Marked increase in left ventricular wall thickness (>30 mm on echocardiography).
- Delayed gadolinium enhancement on cardiac MRI.

Q: What drugs should be **avoided**?

A: As follows:

- Digoxin.
- Vasodilators.
- Diuretics.
- Nitrates.
- Dihydropyridine calcium channel blockers.
- Alcohol (may cause vasodilatation).

Q: What is the effect of HCM in **pregnancy**? What **precautions** should be taken?

A: HCM is not a contraindication to pregnancy. The patient usually tolerates pregnancy well if not severely symptomatic prior to conception. There is no evidence that pregnancy increases the risk of SCD. Following precautions should be taken:

- Prenatal counselling regarding risk of disease in offspring.
- The patient should have regular follow-up in well-equipped centre with expertise in high-risk pregnancies and cardiac disease.
- β-blockers or calcium channel blockers should be continued.

Q: What disease is **associated** with HCM?

A: Friedreich ataxia.

CHAPTER 3

RESPIRATORY SYSTEM

"Work out the best method for examination, and practice it until it is a second nature to you"

–Anonymous

Introduction

Usual instructions by the examiners:

- Examine the respiratory system.
- Examine the chest from front and/or from back.
- Just percuss and auscultate. What are your findings?
- Put your stethoscope here. What are your findings?

Common short cases

- Obvious findings during inspection (e.g. tachypnoea, dyspnoea, lip pursing and thoracic deformity). Puffy, plethoric face with congested eyes [superior vena caval (SVC) obstruction].
- Pleural effusion (unilateral or bilateral).
- Bronchiectasis (unilateral or bilateral).
- Consolidation.
- Collapse of the lung.
- DPLD [previously called interstitial lung disease (ILD) or fibrosing alveolitis].
- Emphysema.
- Pneumothorax.

Examiner may interrupt at any step during examination and ask any question, for example:

What is the **vocal fremitus?** What are the **causes** of increased or decreased vocal fremitus?

What is the **percussion** note? Supposing it is dull, what are the **causes** of dullness on percussion?

What are your **findings** on auscultation? Supposing bronchial sound, what are the **causes** of bronchial sound?

Hence during examination, you must be ready to answer the expected questions. After completing, present the case according to the examiner's instruction, for example:

Present your case or what are your **findings?** (Mention systematically in the form of **inspection, palpation, percussion and auscultation).**

Have you finished? What is your **diagnosis?** (Yes, I have finished my examination. Diagnosis is right-sided pleural effusion.)

Why pleural effusion? (Because Mention the signs of pleural effusion systematically.)

N.B. If asked to examine the back of chest only, ask the patient to keep both hands on the shoulder, i.e. right hand on left shoulder and the left on right. Look for clubbing, any change of joints (rheumatoid arthritis), skin change (systemic sclerosis, dermatomyositis, a good clue for diagnosis, may be associated with ILD).

Examination Routine

Proceed as follows:

- Introduce yourself, remaining on the right side of the patient.
- Undress the patient up to the waist (with permission). The patient should lie flat, but if acutely ill or dyspnoeic, can be examined at 45° or the position in which the patient feels comfortable.
- Look at the patient to see the following points before examination.

If you are asked to examine the respiratory system, the following important **general examinations** are needed:

1. While talking, hoarseness of voice (laryngitis and recurrent laryngeal nerve palsy).
2. Dyspnoeic or orthopnoeic or tachypnoeic (count the respiratory rate).
3. Cough with wheeze (bronchial asthma and chronic obstructive pulmonary disease) or stridor (large airway obstruction).

4. Prominent accessory muscles of respiration [indicates chronic obstructive pulmonary disease (COPD)].
5. Lip pursing (in emphysema).
6. Cyanosis.
7. Cachexic or emaciated [due to tuberculosis (TB), bronchial carcinoma, lean and thin in emphysema], obesity (associated with sleep apnoea syndrome).
8. Raised jugular venous pressure (JVP) (cor pulmonale) or SVC obstruction.
9. In the face:
 - Pink puffer (due to emphysema).
 - Blue bloater (due to chronic bronchitis).
 - Puffy, oedematous, plethoric and red eye (SVC obstruction).
 - Skin change (systemic sclerosis).
 - Butterfly rash [dermatomyositis and systemic lupus erythematosus (SLE)].
 - Eye with Horner syndrome (partial ptosis and constricted pupil) in Pancoast tumour.
10. In the hands:
 - Nicotine staining in nails (may be associated with bronchial carcinoma).
 - Clubbing.
 - Cyanosis.
 - Wasting (due to involvement of lower trunk of brachial plexus by bronchial carcinoma, C8 and T1 lesions).
 - Pulse: Tachycardia, pulsus paradoxus (due to severe obstructive airway disease), high-volume and bounding pulse (due to CO_2 excess).
 - Warm and sweaty hands (due to anoxic cor pulmonale).
 - Flapping tremor (due to severe respiratory failure and CO_2 retention).
 - Other diseases involving the hands, such as rheumatoid arthritis and systemic sclerosis (all can cause fibrosing alveolitis).
11. In the legs:
 - Oedema (cor pulmonale).
 - Deep vein thrombosis (DVT) can cause pulmonary embolism.
 - Clubbing and cyanosis.
12. Heart (to see evidence of pulmonary hypertension and cor pulmonale).
13. In the abdomen:
 - Liver (cor pulmonale).
 - See, if paradoxically abdomen shows inward motion during inspiration (which indicates diaphragmatic paralysis).
14. Lymph nodes (lymphoma, metastasis, TB and sarcoidosis).

Examination of the Chest

(Examination should be performed systematically: **Inspection, palpation, percussion** and **auscultation;** and, also present the case in the same way. Always examine both front and back of chest and compare both right and left side during each part of examination.)

Inspection:

- Shape of chest (asymmetry or deformity or kyphoscoliosis, pectus excavatum or carinatum), flattening and drooping of the shoulder (fibrosis or collapse).
- Movement of chest (unilateral or bilateral restriction), movement upward (in emphysema). See paradoxical inward motion of abdomen during inspiration with the patient in supine position (indicates diaphragmatic paralysis).
- Intercostal space (ICS) (fullness, indrawing of lower ribs).
- Scar marks (thoracotomy scar and thoracoplasty) and radiation marks.
- Visible impulse (cardiac impulse and epigastric pulsation).
- Visible, engorged vein in chest (SVC obstruction).
- Others: Suprasternal and supraclavicular excavation (hyperinflation), prominent accessory muscles, gynaecomastia, needle puncture mark and tattooing.

Palpation:

- Position of trachea (central, deviated to right or left).
- Apex beat.
- Vocal fremitus.
- Chest expansion.
- Tracheal tug (descent of trachea during inspiration, examine by placing fingers over the trachea; it indicates hyperinflation).
- Cricosternal distance is the distance between suprasternal notch and cricoid cartilage (normally, three fingers or more. If it is less, indicates hyperinflation).
- Rib tenderness (due to trauma or fracture, secondary deposit), tenderness in costochondral junction (due to Tietze syndrome).

Percussion:

- Percussion note (normal resonance, hyperresonance or stony dull or woody dull, impaired).
- Area of liver dullness (normally in right sixth rib or fifth intercostal space in midclavicular line, obliterated or lower down in emphysema or severe asthma).
- Area of cardiac dullness (obliterated due to emphysema or severe asthma).

Auscultation:

(Turn the head of the patient to the left side and tell him, 'Keep your mouth open, take deep breath in and out for me'. Place the stethoscope, and check both right and left side alternately.)

- Breath sounds (normal vesicular, vesicular with prolonged expiration and bronchial).
- Vocal resonance (normal, increased, decreased or absent).
- Added sounds:
 - Rhonchi (high or low pitched, localized or generalized).
 - Pleural rub.
 - Crepitations (fine or coarse or end inspiratory. If crepitations are present, ask the patient to cough and see again). Posttussive crepitation (appears after cough) sometimes found after cough due to TB.

Now ask the patient to sit forward, and examine back of chest systematically.

Finally, see the following points:

- If your diagnosis is COPD, see forced expiratory time (FET) by asking the patient to exhale forcefully after full inspiration, while you listen by placing your stethoscope over the trachea.
- Normally, it is <6 s; >6 s indicates airway obstruction.
- Finally, if any sputum cup is available nearby, look at the sputum and comment on it.

Discussions on Routine Examination

Respiratory Rate

- Normally, it is 14–18/min (in adult).
- Increased rate of respiration is called tachypnoea (>20). Usually, it is faster in children, slower in the elderly.
- Increased depth of respiration is called hyperpnoea.

Causes of **tachypnoea** (increased rate of respiration):

1. Physiological: Anxiety, fear, exercise or exertion.
2. Pathological:
 - Respiratory causes (bronchial asthma, pneumonia or other respiratory infections, pulmonary embolism, COPD).
 - Cardiac causes [acute anterior myocardial infarction (MI), acute left ventricular failure, left ventricular failure (LVF)].
 - Others: Fever, metabolic acidosis (diabetic ketoacidosis, lactic acidosis and renal failure), hysterical conversion reaction (HCR) and cerebrovascular accident (CVA).

Causes of **reduced** respiratory rate:

- Sleep.
- Depression of respiratory centre (by narcotic drugs, in some CVD).

N.B. Remember the following points:

- Normally, respiration in male is abdomino-thoracic (as man uses diaphragm more than intercostal muscles).
- Respiration in female is thoracoabdominal (as woman uses intercostal muscles more than diaphragm). In babies, it is abdominal (diaphragmatic).
- If respiratory movement is **exclusively abdominal,** think of the following causes: Ankylosing spondylitis, intercostal muscle paralysis, pleuritic pain or any painful condition of chest.
- If respiratory movement is **exclusively thoracic,** it indicates reduced diaphragmatic movement due to peritonitis, ascites and pregnancy.

Abnormal Breathing

Kussmaul breathing (air hunger): It is characterized by deep, sighing, rapid respiration at regular rate due to stimulation of respiratory centre. Its causes are (due to metabolic acidosis):

- Diabetic ketoacidosis.
- Renal failure.

(Occasionally in severe respiratory failure and hepatic failure.)

Ataxic breathing (Biot breathing): Characterized by irregular respiration in timing and depth. It indicates brain stem damage (CVA and head injury).

Cheyne–Stokes breathing: Cyclical variation in the depth of respiration characterized by gradual deepening of respiration till a maximum is attained, followed by gradual diminished respiration until a period of apnoea occurs (apnoea alternates with hyperpnoea). It is due to diminished sensitivity of respiratory centre to CO_2. This cycle may last for 2 min. Its causes are:

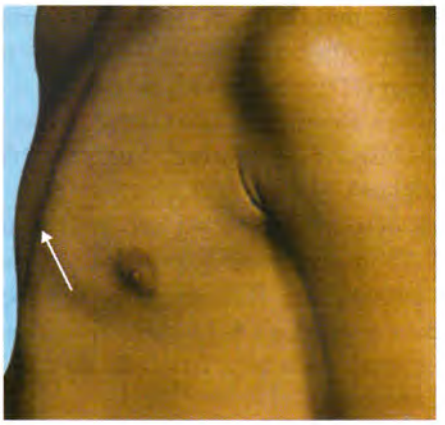
- Acute LVF (or severe heart failure).
- Coma due to any cause.
- Brain damage due to head injury and cerebral haemorrhage.
- Narcotic drug poisoning.
- Sometimes, at high altitude.

Apneustic breathing: Characterized by a postinspiratory pause in breathing. It indicates pontine damage.

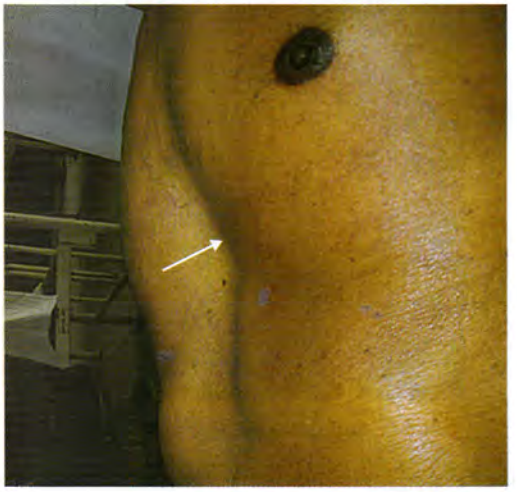
Paradoxical breathing: If abdomen sucks inward during inspiration. It indicates diaphragmatic paralysis.

Shape of the Chest (Deformity or Asymmetry)

1. **Asymmetry:** It may occur due to kyphosis, scoliosis or lordosis, and flattening.
2. **Pigeon chest (pectus carinatum):** It is the localized prominence, outward bowing of sternum and costal cartilage. Its causes are:
 - Congenital.
 - Rickets.
 - Marfan syndrome.
 - Homocystinuria.
 - Repeated respiratory infection in childhood (causing strong diaphragmatic contraction as the thorax still remains pliable).
 - Bronchial asthma since childhood.
 - Osteogenesis imperfecta.
3. **Pectus excavatum** (funnel chest, saucer or cup): It is the localized depression at the lower end of sternum or rarely depression of whole length of the body of sternum and of costal cartilage attached to it. It does not usually cause any problem; rarely, it may cause lung and cardiac problems (pulmonary hypertension and cor pulmonale). Its causes are:
 - Congenital (common cause).
 - Rickets.
 - Marfan syndrome.
 - Homocystinuria.
 - Osteogenesis imperfecta.



Pectus carinatum



Pectus excavatum



Harrison sulcus

4. **Harrison sulcus:** It is a groove directed outwards and slightly downwards from sternum in the lower part of the chest anteriorly, along the line of attachment of diaphragm (due to indrawing of ribs). Its causes are:
 - Chronic bronchial asthma since childhood.
 - Rickets.

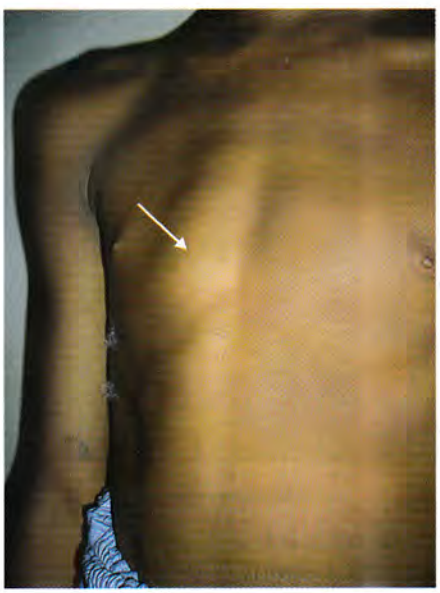
5. **Barrel-shaped chest:** In this type, anteroposterior diameter of the chest is increased than the transverse diameter (TD), ribs look more horizontal, intercostal spaces appear full, chest remains like the stage of full inspiration, subcostal angle >90° (normally 90° or less).

 It is detected by placing two hard boards—one on the front and another on the back of the chest—and measure the distance between these two for anterior–posterior (A–P) diameter (normal ratio of A:P diameter is 5:7). Its causes are:
 - Emphysema.
 - Severe chronic asthma.



Barrel-shaped chest

6. **Rickety rosary:** It is the prominent swelling at the costochondral junction due to rickets.



Rickety rosary

7. **Flail chest:** It occurs in multiple fractures of ribs and sternum. There is paradoxical movement of chest inwards during inspiration.

8. **Thoracoplasty:** In this procedure, some ribs are resected on one side of the chest to achieve permanent collapse of the lung. Usually one side of the upper part of the chest is depressed. Previously, it was done to treat pulmonary tuberculosis (before the development of chemotherapy).

Reduction of Movement of Chest

Any respiratory disease is associated with reduction of movement on the affected side. Causes of **restricted** or **reduction** of movement:

1. Unilateral:
 - Pleural effusion.
 - Pneumothorax.
 - Collapse.
 - Fibrosis.
 - Consolidation.
2. Bilateral:
 - COPD (especially in emphysema).
 - Diffuse pulmonary fibrosis.

Expansion of the Chest

It is measured by placing the hands in lower part of the chest (also in middle part), fingers are placed on the side of chest keeping the thumbs in midline and close to each other (can also be measured using tape at the level of nipple). Ask the patient to take a deep breath in and out. Normal expansion is >5 cm.

Causes of **reduced** expansibility:

- Emphysema (in severe emphysema, it is <1 cm).
- Pleurisy.
- Ankylosing spondylitis.
- Respiratory muscle paralysis.

Trachea

Normally, it is slightly deviated to the right. Causes of **shifting** of trachea on:

1. Same side (on the side of lesion):
 - Collapse.
 - Fibrosis.
 - Pneumonectomy.
2. Opposite side (opposite to the side of lesion):
 - Pleural effusion.
 - Pneumothorax.

Apex Beat

May be shifted, causes are as in trachea (see above). (Apex beat is also shifted in kyphoscoliosis, pectus excavatum and cardiac cause.)

N.B. Remember the following points:

- Trachea may be shifted in retrosternal goitre.
- Level of tracheal bifurcation: At the lower end of manubrium sterni (angle of Louis) in front and between fourth and fifth thoracic vertebrae behind. Shifting of apex beat and trachea indicates mediastinal shifting. However, these may not be shifted, if mediastinum is **fixed** due to idiopathic fibrosing mediastinitis, radiotherapy or methysergide therapy.

Vocal Fremitus

Maybe normal, or increased or decreased (less practised, as vocal resonance is more sensitive).

Causes of increased vocal fremitus (three Cs)

- Consolidation.
- Collapse with patent bronchus.
- Cavity (large).
- Also in fibrosis.

Causes of decreased vocal fremitus

- Pleural effusion.
- Thickened pleura.
- Pneumothorax.
- Collapse with complete bronchial obstruction.
- Mass lesion (bronchial carcinoma and hydatid cyst).

Percussion

Percussion note may be normal resonance, hyperresonance, dull or stony dull.

Causes of hyperresonance

- Pneumothorax.
- Big cavity.
- Big bullae.
- Emphysema (usually increase resonance).

Causes of dullness

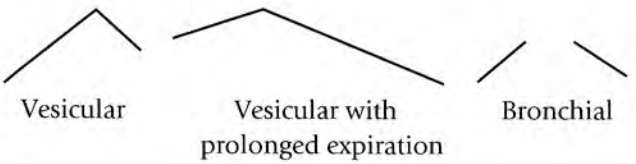
- Pleural effusion (stony dull).
- Thickened pleura (impaired dull).
- Consolidation (woody dull).
- Collapse.
- Mass lesion.
- Raised diaphragm due to hepatomegaly (dullness on the right side)

Auscultation

Listen to the breath sound, compare on both sides using the diaphragm of stethoscope. Use the bell above the clavicle to hear lung apices.

Breath sound may be normal (vesicular), bronchial, vesicular with prolonged expiration, diminished or absent.

1. **Normal vesicular** (similar to wind rustling in leaves): It is louder and longer in inspiration, and expiration is short, without any gap. Vesicular sound is produced in large airways. When heard through normal lung, filtering effect through the alveoli produces attenuated and low-pitched sound.



2. **Bronchial:** Harsh, louder, blowing quality, inspiration and expiration are of similar length and intensity with a gap in between inspiration and expiration. It is produced in large airways, but when the lung between airway and chest wall is airless (e.g. consolidation), loss of filtration effect results in high-pitched bronchial sound. Bronchial sounds are of two types:
 - High-pitched (tubular): Found in consolidation and collapse with patent bronchus.
 - Low-pitched (also called cavernous): Found in cavitation.

 Causes of bronchial sound (three Cs)
 - Consolidation.
 - Collapse with patent bronchus.
 - Cavity (nearer chest wall).
 - Also fibrosis (low pitched).
3. Causes of **vesicular with prolonged** expiration:
 - COPD (chronic bronchitis and emphysema).
 - Bronchial asthma.

Vocal Resonance

This may be normal, increased or decreased. Vocal resonances are of three types:

- Bronchophony: It appears to be near the ear piece, and found in consolidation.
- Aegophony: Nasal quality or goat-like (Greek: *aix* means goat and *phony* means sound), found in consolidation and above the fluid level of pleural effusion.
- Whispering pectoriloquy: Ask the patient to tell **'ninety-nine' or 'one-one one'**, as if whisper.

When auscultated with stethoscope, it appears as if the patient whispers in the examiner's ear. It may be found in consolidation, collapse or cavitation (three Cs).

N.B. If bronchial sound is present, whispering pectoriloquy is also present. Hence, always auscultate for whispering pectoriloquy.

Causes of increased vocal resonance (three Cs)

- Consolidation.
- Collapse with patent bronchus.
- Cavity.
- Also in fibrosis.

Causes of decreased vocal resonance

- Pleural effusion.
- Thickened pleura.
- Pneumothorax.
- Collapse with complete bronchial obstruction.
- Mass lesion.

Added Sounds

- Pleural rub.
- Crepitation.
- Rhonchi.

Pleural Rub

- It is a localized grating, creaking, rubbing and leathery sound produced by movement of visceral pleura over parietal pleura.
- Heard both in inspiration and expiration, disappears when breathing is hold.
- The rub is augmented by pressing the stethoscope.
- May be palpable and associated with local pain.

Presence of pleural rub indicates pleurisy (which may be due to viral or other infections, pneumonia, pulmonary infarction and bronchial carcinoma).

Pleuropericardial rub:

- When pleurisy involves the pleura adjacent to pericardium, pleuropericardial rub is heard (there is no pericarditis).
- It is due to rough pleural surface adjacent to pericardium, which moves across one upon another by cardiac pulsation.

Q: What are the **differences** between pleural rub and pericardial rub?

A: As follows:

Pleural rub	Pericardial rub
Anywhere on chest	Over precordium, but better in left lower parasternal area (bare area of the heart)
Absent, if respiration is stopped	No relation with respiration
It is due to pleurisy	It is due to pericarditis

Crepitations

These are bubbling or crackling sounds, occur due to passage of air through fluid in alveoli. Crepitations may be fine or coarse; present in inspiration, expiration or both.

- Early inspiratory crepitations, commonly found in chronic bronchitis.
- End or pan-inspiratory crepitations, found in fibrosing alveolitis.

Causes of **coarse crepitation** (see also page 141):

- Bronchiectasis.
- Resolution stage of pneumonia.

Crepitations **reduce** or **disappear** after coughing in the following diseases:

- Resolving pneumonia.
- Bronchiectasis.
- Lung abscess.
- Pulmonary oedema.

Crepitation **not changed** after coughing is found in:

- DPLD.

Q: Why **end-inspiratory** coarse crepitation in DPLD?

A: It is due to reopening of collapsed alveoli at the end of inspiration (not due to fluid in alveoli).

Q: What are the **differences** between pleural rub and crepitation?

A: As follows:

Pleural rub	Crepitation
It is grating or creaking or rubbing sound	Bubbling or crackling sound
No change with cough	Changes with cough
It may be palpable	Not palpable
Augmented by pressing stethoscope	Not so
Local pain due to pleurisy	No local pain

Rhonchi

It is the musical sound produced by passage of air through narrow airways (due to mucosal oedema or spasm of bronchial musculature). It is of two **types**:

- High pitched: Indicates small airway obstruction.
- Low pitched: Indicates large bronchi obstruction.

Causes of rhonchi:

- Bronchial asthma (medium or high pitched, more in expiration).
- Chronic bronchitis (low or medium pitched, both in inspiration and expiration).

Localized rhonchi (indicates partial obstruction of large bronchus); usually a fixed, low-pitched rhonchi. Its causes are:

- Neoplasm (bronchial carcinoma and adenoma).
- Foreign body.
- Mucous plugs (disappear after coughing).
- Congenital bronchial stenosis.

Bedside Lung Function Tests

- **FET** (forced expiratory time): Ask the patient to exhale forcefully after full inspiration while you listen by placing your stethoscope over the trachea. Normally, patient can empty in <6 s. If >6 s, indicates airway obstruction (remember the age, add 1 s for every decade, e.g. a 40-year-old person can exhale in 4 s).
- **PEFR** (peak expiratory flow rate): Done using Wright peak flow meter. Normally in young males, it is 600 L/min; and in females, 400 L/min (value varies with age, sex and height; hence, the table for the normal value should be seen). It is reduced in COPD and bronchial asthma.

Drug-induced Lung Disease

1. **Drugs that cause or aggravate bronchial asthma:**
 - β-Blockers.
 - Aspirin and other NSAIDs.
 - Tamoxifen.
 - Dipyridamole.
 - Nebulized pentamidine [used for treatment of *Pneumocystis carinii* (*now called Pneumocystis jiroveci*) infection].
2. **Drugs causing cough:**
 - ACE inhibitors (the commonest cause, more in females; actual mechanism is unknown). This drug causes conversion of angiotensin-1 to angiotensin-2. Also, causes breakdown of bradykinin and substance P. All these may cause cough.
3. **DPLD (noneosinophilic alveolitis):**
 - Busulphan.
 - Bleomycin.
 - Methotrexate.
 - Amiodarone.
 - Nitrofurantoin.
 - Azathioprine.
4. **Pulmonary eosinophilia:**
 - Antibiotics (sulphonamide, penicillin, tetracycline and nitrofurantoin).
 - Antirheumatic agent (gold, aspirin, penicillamine and naproxen).
 - Anticonvulsant (phenytoin and carbamazepine).
 - Antidepressant or antipsychotic (imipramine, chlorpromazine and dothiepin).
 - Cytotoxic (methotrexate, bleomycin and procarbazine).
5. **Acute respiratory distress syndrome (ARDS):**
 - Aspirin and opium (in overdose).
 - Streptokinase.
 - Hydrochlorothiazide.
6. **Pleural disease or effusion:**
 - Bromocriptine.
 - Nitrofurantoin.
 - Methotrexate.
 - Methysergide.
 - By SLE (hydralazine, INH, procainamide, phenytoin, carbamazepine and chlorpromazine).
7. **Mediastinal widening or hilar lymphadenopathy (pseudolymphoma):**
 - Phenytoin or diphenylhydantoin.
8. **Respiratory failure:**
 - Opium.
 - Sedative or hypnotic.
 - Alcohol.
 - Tricyclic antidepressant.

Q: What is **dyspnoea?**

A: It is the unpleasant, subjective awareness of breathing.

Causes of **acute or sudden dyspnoea:**

- Acute severe asthma.
- Pulmonary oedema (acute LVF).
- Pulmonary embolism.
- Spontaneous pneumothorax.
- Adult respiratory distress syndrome.
- Hysterical conversion reaction (HCR) or panic attack.

Cause of **dyspnoea on supine:**

- Phrenic nerve palsy (bilateral diaphragmatic paralysis).

Platypnoea: It means dyspnoea that worsens on upright position. It occurs in arteriovenous (AV) malformation at lung bases resulting in increased shunting and hypoxia in upright position.

Crepitation or Pleural Rub

Usual instructions:

- Put your stethoscope here (on chest). What is your finding?

Presentation of a Case: 1

- There is pleural rub (tell the site).

Q: Describe pleural rub.
A: It is a localized scratchy, grating, cracking, rubbing or leathery sound produced by movement of visceral pleura over parietal pleura, augmented by pressing the stethoscope. It is present both in inspiration and expiration, and disappears when breathing is stopped. It may be palpable and associated with local pain.

Q: What does it **indicate**?
A: Pleurisy.

Q: What are the **causes** of pleurisy?
A: It may be due to viral (commonly coxsackie B) or other infections, pneumonia, pulmonary infarction and bronchial carcinoma.

Q: What is patient's **complaint**?
A: Pleuritic chest pain that is characterized by sharp, localized pain which is aggravated by coughing, deep breathing, change of posture and movement.

Q: What is the **differential diagnosis** of pleural rub?
A: Crepitation.

Presentation of a Case: 2

- There are multiple crepitations (mention fine or coarse) present in both inspiration and expiration (mention whether unilateral or bilateral, and the site).

Q: What do you think the **cause** of crepitation?
A: As follows (mention according to unilateral or bilateral):

If **unilateral**, causes are:
- Bronchiectasis.
- Resolution stage of pneumonia.
- Lung abscess.

If **bilateral**, causes are:
- Bilateral bronchiectasis.
- Pulmonary oedema.
- DPLD.

Q: What is **crepitation**?
A: These are bubbling or crackling sounds that occur due to passage of air through fluid in alveoli. Crepitations may be fine or coarse, present in inspiration, expiration or both.

Q: How to **differentiate** between pleural rub and crepitation?
A: See on the page 128.

Q: What are the **differences** between pleural rub and pericardial rub?
A: See on the page 128.

Pleural Effusion

Most signs are easily found by examining the chest from back, especially in small effusion. Look for any needle puncture mark, local dressing with gauze and tape and any scar mark, and mention it.

Presentation of a Case

(Supposing right-sided, tell the findings in right side)

On inspection:
- Restricted movement.
 (There is one puncture mark, gauze and tape, mention if any.)

On palpation:
- Trachea and apex beat: Shifted to the left side.
- Vocal fremitus: Reduced or absent in right side (up to ..., mention the location).
- Chest expansion is reduced.

On percussion:
- Stony dullness (up to ..., mention the location).

On auscultation:
- Breath sound: Diminished or absent.
- Vocal resonance: Diminished or absent.
- No added sound.

My diagnosis is **right-sided pleural effusion.**

Q: What are the **differential diagnoses?**
A: As follows:
- Thickened pleura.
- Mass lesion.

Q: Why this is not **thickened pleura?**
A: In thickened pleura, no mediastinal shifting and dullness is impaired.

Q: Why not this is **consolidation?**
A: In consolidation, dullness is woody, there is no shifting of mediastinum, bronchial sound is present and vocal resonance is increased.

Q: Why not this is **collapse?**
A: In collapse, the apex beat and trachea will be shifted to the same side (also, in collapse with patent bronchus, there is bronchial breath sound and increase vocal resonance).

Q: Why not **pneumothorax?**
A: In pneumothorax, there is hyperresonance on percussion.

N.B. Just above the upper level of effusion, the following findings may be present (due to compression collapse of lung):

- Bronchial sound.
- Increased vocal resonance.
- Whispering pectoriloquy.
- Pleural rub.

Q: What is **pleural effusion?**
A: Accumulation of excessive amount of fluid in pleural cavity is called pleural effusion.

Q: Can there be **chest pain** in pleural effusion?
A: Chest pain may occur due to pleurisy (may be present in mild effusion).

Q: What are the **characteristics** of pleuritic chest pain?
A: Pleuritic chest pain is localized, sharp or lancinating in nature—worse on coughing, deep inspiration or movement.

Q: What are the causes of **dullness on percussion** over lower chest?
A: As follows:

- Pleural effusion (stony dullness).
- Thickened pleura.
- Consolidation (woody dullness).
- Collapse of the lung.
- Raised right hemidiaphragm (due to hepatomegaly or liver pushed up).
- Mass lesion.

Q: What are the **definitive signs** of pleural effusion?
A: Stony dullness and reduced or absent breath sound (confirm by aspiration).

Q: What do you think of the **causes** of pleural effusion in this case?
A: Mention the causes considering the age and sex, in the following way:

If the patient is young, the causes are:

- Common causes: Pulmonary TB and parapneumonic.
- Others: Lymphoma and SLE in female (also pulmonary infarction).

If the patient is middle-aged or elderly, the causes are:

- Pulmonary TB.
- Parapneumonic.
- Bronchial carcinoma.

Four common causes of pleural effusion:

- Pulmonary TB.
- Parapneumonic.
- Bronchial carcinoma.
- Pulmonary infarction.

N.B. Remember the following points in pleural effusion:

- Pleural fluid normally present: 5–15 mL.
- At least, 500 mL of fluid is necessary to detect clinically.
- At least, 300 mL of fluid is necessary to detect radiologically in PA view.
- At least, 100 mL of fluid is necessary to detect radiologically in lateral decubitus position.
- Less than 100 mL or small amount of fluid is detected by ultrasonography (even 20–25 mL fluid can be detected).

Q: How to **confirm** if there is small effusion? (If not detected by chest X-ray, PA view.)
A: By doing:

- X-ray in lateral decubitus position.
- Ultrasonogram (USG) of lower part of the chest.
- Occasionally, CT scan of chest may be needed.

Q: If **clinically** pleural effusion, but there is **no fluid** during aspiration, then mention the **causes.**
A: As follows:

- Fluid may be thick (empyema).
- Thickened pleura.
- Mass lesion.

Q: What are the causes of predominantly **right-** or **left-sided** pleural effusion?
A: As follows:

Causes of **right-sided pleural effusion:**

- Liver abscess.
- Meigs syndrome.
- Dengue haemorrhagic fever.

Causes of **left-sided pleural effusion:**

- Acute pancreatitis.
- Rheumatoid arthritis.
- Dressler syndrome.
- Oesophageal rupture (Boerhaave syndrome).
- Dissecting aneurysm.

Q: What are the **types** of pleural effusion according to the colour?

A: According to colour, pleural effusion may be:

- Serous (hydrothorax).
- Straw.
- Purulent (empyema or pyothorax).
- Haemorrhagic (haemothorax).
- Milky or chylous (chylothorax).



Haemorrhagic



Straw colour



Serous



Chylous

N.B. Clinically, only pleural effusion should be mentioned. After drawing the fluid and according to its colour, other diagnosis may be done, e.g. if pus, it is empyema.

Q: What **investigations** will you do in pleural effusion?

A: Mention according to the age of patient and suspected cause:

1. Chest X-ray PA view (if small effusion, lateral decubitus view).
2. Hb%, total count (TC), differential count (DC), erythrocyte sedimentation rate (ESR) (high ESR in TB, leucocytosis in pneumonia).
3. Mantoux test (MT).
4. Aspiration of fluid for analysis:
 - Physical appearance (straw coloured, serous, haemorrhagic and chylous).
 - Gram staining, cytology (routine) and exfoliative cytology (malignant cells).
 - Biochemistry (protein and sugar); also a simultaneous blood sugar, protein and lactate dehydrogenase (LDH) may be done.
 - Adenosine deaminase (ADA) (high in tuberculosis).
 - Culture and sensitivity (C/S).
 - Acid-fast bacilli (AFB) and mycobacterial C/S.
5. Others (of pleural fluid), according to suspicion of causes:
 - Cholesterol, LDH and rheumatoid factor (in RA).
 - Amylase (high in acute pancreatitis, oesophageal rupture and malignancy).
 - Triglyceride (in chylothorax).
6. Pleural biopsy by Abram or Cope needle (positive in 80% cases with TB and 40–60% cases with bronchial carcinoma).
7. If cough, sputum for Gram staining, C/S, AFB and mycobacterial C/S, and malignant cells (exfoliative cytology).
8. If palpable lymph node, fine-needle aspiration cytology (FNAC) or biopsy (for lymphoma, metastasis).
9. Other investigations according to suspicion of causes include:
 - ANF, anti-double stranded DNA (SLE).
 - Liver function test (LFT) [chronic liver disease (CLD)].
 - Urine for protein and serum total protein (nephrotic syndrome).
10. CT scan in some cases (it helps to clarify pleural abnormalities more readily than chest X-ray and ultrasonogram; and also helps to distinguish between benign and malignant diseases).



Right-sided pleural effusion

Q: What is the role of **pleural fluid amylase?**

A: Pleural fluid amylase may be higher than serum amylase in acute pancreatitis, bacterial pneumonia, oesophageal rupture and malignancy. It is high in adenocarcinoma of lung and may be useful in differentiating it from mesothelioma.

Q: What are the causes of **high eosinophil** in the pleural fluid (also high in the blood)?

A: Pulmonary eosinophilia, polyarteritis nodosa and rarely lymphoedema.

N.B. Presence of high eosinophil in pleural fluid, but not in blood is likely due to pulmonary embolism. High eosinophil in pleural fluid is unlikely to be malignant.

Q: How to **differentiate** between exudative and transudative pleural effusion?

A: As follows:

Criteria	Exudative	Transudative
Appearance	Straw, purulent, hazy, chylus or blood stained	Clear or serous
Protein	>3 g%	<3 g%
Glucose	Low	Normal
Cholesterol	>60 mg/dl	<60 mg/dl
LDH	Greater than two-thirds of the upper limit of normal serum LDH	Less than two-thirds of the upper limit of normal serum LDH.
Pleural fluid LDH: Serum LDH	>0.6	<0.6
Pleural fluid protein: Serum protein	>0.5	<0.5
Serum-effusion albumin gradient (serum albumin – pleural fluid albumin)	<1.2 g/dl	>1.2 g/d

N.B. Remember the following:

- Pleural fluid cholesterol level <60 mg/dl indicates transudate. In all malignant effusion, pleural fluid cholesterol > 60 mg/dl. So, this test is useful to separate these two types of effusion.
- High pleural fluid ADA indicates tubercular pleural effusion.

Read the Following Topics in Relation to Pleural Effusion

Causes of pleural effusion: There are two types: **Exudative** and **transudative.**

1. **Exudative** (protein >3 gm%):
 - Pulmonary TB.
 - Pneumonia.
 - Bronchial carcinoma.
 - Pulmonary infarction.
 - Collagen diseases (SLE and RA).
 - Lymphoma.
 - Dressler syndrome [postmyocardial infarction (post-MI) syndrome characterized by pain, pyrexia, pericarditis, pleurisy and pneumonitis].
 - Others (acute pancreatitis, subphrenic abscess, liver abscess, pleural mesothelioma, secondaries and yellow nail syndrome).
2. **Transudative** (protein <3 gm%):
 - Congestive cardiac failure (CCF).
 - Nephrotic syndrome.
 - Cirrhosis of liver.
 - Malnutrition.
 - Hypothyroidism.
 - Meigs syndrome (ovarian fibroma, ascites and right-sided pleural effusion).
 - Chronic constrictive pericarditis.
 - Acute rheumatic fever.

Q: What is **pseudotumour (phantom tumour)?**

A: It is the accumulation of fluid in interlobular fissure, usually found along the lateral chest wall. Chest X-ray shows rounded homogeneous opacity, misdiagnosed as a tumour. It is confirmed by ultrasonography (USG) (localized or encysted effusion) or CT scan. It disappears with resolution of effusion. It is commonly found in CCF.

Q: What is **yellow nail syndrome?**

A: It is a congenital disorder characterized by:

- Nails: Yellow, thick, onycholysis.
- Lymphoedema of legs.
- Pleural effusion or bronchiectasis.

Q: What are the features of **parapneumonic effusion?** How to **treat?**

A: Usually small and localized, and may be noninfected or infected fluid. Any loculated effusion is highly suggestive of empyema.

Treatment:

1. Uncomplicated parapneumonic effusion is treated with antibiotic.
2. Complicated parapneumonic effusion: Thoracotomy tube should be inserted in the following situations:
 - Gross pus.
 - Gram staining of fluid shows positive organism.
 - Glucose is <50 mg/dL.
 - pH < 7.00.
3. If pleural fluid is loculated and not adequately drained, then give streptokinase injection 250,000. Or, urokinase 100,000 units should be injected intrapleurally to dissolve fibrin membrane.
4. If still inadequate drainage, thoracoscopy with breakdown of adhesion or thoracotomy with decortication should be done.

Q: How can you **suspect malignant effusion?**

A: Elderly emaciated patient with clubbing and nicotine stain, palpable lymph node and radiation mark in chest. Pleural fluid is haemorrhagic and there is rapid accumulation after aspiration.

Causes of haemothorax (blood-stained fluid):

- Chest injury or trauma.
- Bronchial carcinoma.
- Pleural mesothelioma.
- Pulmonary infarction.
- Others: SLE, lymphoma and acute pancreatitis.

Differences between traumatic haemothorax and haemorrhagic pleural effusion

Traumatic haemothorax	Haemorrhagic pleural effusion
Less uniform	Uniformly mixed
Usually clots on standing	Does not clot
Gross haemorrhage, RBC > 100,000/mm^3	RBC > 10,000/mm^3
RBC not crenated (fresh RBC)	RBC may be crenated

Causes of empyema:

- Bacterial pneumonia.
- Lung abscess (bursting in pleural cavity).
- Bronchiectasis.
- TB.
- Secondary infection after aspiration.
- Rupture of subphrenic abscess or liver abscess.
- Infected haemothorax.

Q: How to diagnose **empyema thoracis** clinically?

A: As follows:

- High fever, sometimes hectic, may be associated with chill, rigor and sweating. Fever is persistent or recurrent despite treatment with a suitable antibiotic.
- Malaise, weight loss.
- Pleuritic chest pain, breathlessness.
- Copious purulent sputum if empyema ruptures into a bronchus (bronchopleural fistula).
- Toxic, emaciated.
- Tachypnoea.
- Tachycardia.
- Features of pleural effusion.
- Clubbing.
- To be confirmed: Aspiration that shows pus or purulent fluid.

Q: What is **empyema necessitans?**

A: In empyema thoracis, fluid may come out subcutaneously in the chest wall. This is called empyema necessitans.

Characteristics of empyema fluid:

- Fluid is purulent.
- Thick.
- Biochemical: Glucose low, <3.3 mmol/L, protein exudative, LDH > 1000 U/L.
- C/S: Organism may be found.
- Pleural biopsy may be done to exclude tuberculosis.

Q: What is the **treatment** of empyema thoracis?

A: According to cause:

1. Nontuberculous:
 - Drainage of pus with wide bore intercostal tube using water seal drainage.
 - Antibiotic for 2–6 weeks. I/V co-amoxiclav or cefuroxime plus metronidazole. May be given according to C/S.
 - Surgical intervention if pus is thick or loculated. Surgical decortication of the lung may be needed, if visceral pleura are grossly thickened.
2. Tuberculous empyema:
 - Antitubercular drug.
 - Wide-bore needle aspiration or intercostal tube drainage.
 - Sometimes surgical ablation of pleura.

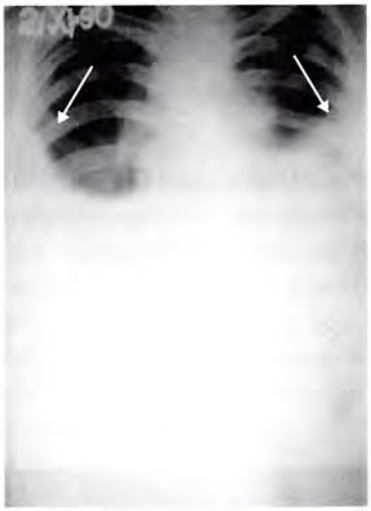
Causes of bilateral effusion:

- All causes of transudative effusion (CCF, nephrotic syndrome, cirrhosis of liver, malabsorption or malnutrition or hypoproteinaemia).
- Collagen diseases (rheumatoid arthritis and SLE).
- Lymphoma.
- Bilateral extensive pulmonary TB.
- Pulmonary infarction.
- Malignancy (usually multiple metastases involving both lungs).

Causes of recurrent pleural effusion:

- Bronchial carcinoma (the commonest cause).
- Pleural mesothelioma.
- Lymphoma.
- Collagen disease (SLE).
- All causes of transudate.

Treatment of recurrent effusion: By pleurodesis.



Bilateral pleural effusion

Q: How is **pleurodesis** done?

A: In the following way:

- A plain rubber tube is introduced in the intercostal space and fluid is removed as far as possible. Introduce the drug, tetracycline (500 mg) or kaolin or talc through the tube, clamp it and keep for 4–8 h (may be overnight). In malignant pleural effusion, bleomycin 30–60 mg is introduced.
- Patient's posture should be changed 2 hourly to allow the drug to spread in pleural space.
- After 4–8 h, remove any remaining fluid and take out the drainage tube at the height of inspiration.
- The patient usually complains of severe chest pain after pleurodesis. In such case, analgesic should be given.

Causes of chylothorax (milky or whitish fluid due to lymph) are injury or obstruction of thoracic duct due to any of the following causes:

- Traumatic (surgery and trauma to the thoracic duct).
- Neoplastic (bronchial carcinoma and metastasis).
- Infective (TB and filariasis).
- Lymphoma involving thoracic duct.

Q: How to **differentiate** between chylothorax and empyema?

A: In both cases, fluid may be cloudy. It is centrifuged and following is observed:

- If clear, empyema.
- If persistently cloudy or milky, chylothorax.

Q: What are the **mechanisms** of pleural effusion?

A: Excess pleural fluid accumulation occurs when pleural fluid formation exceeds absorption or normal pleural fluid formation with reduced absorption. Probable mechanisms are:

- Increased hydrostatic pressure (as in CCF).
- Reduced plasma colloidal osmotic pressure (as in hypoproteinaemia).
- Involvement of pleura causing increased permeability (as in TB and tumour).
- Impaired lymphatic drainage of pleural space (as in obstruction of lymphatic system by tumour, TB and radiation).
- Transdiaphragmatic passage of fluid (in liver disease, ascites and acute pancreatitis).

Q: What is the **mechanism** of tuberculous pleural effusion?

A: Hypersensitivity to tuberculous protein in pleural space.

Q: What is **subpulmonary** pleural effusion?

A: Effusion between the lower surface of lung and upper surface of diaphragm. Confused with subphrenic abscess. Detected by chest X-ray in lateral decubitus position, or USG or CT scan.

Features of rheumatoid pleural effusion

1. Common in male.
2. Occurs in 3% cases of RA.
3. Usually small effusion, more in left side (cause unknown), may be bilateral.
4. Pleural fluid is never blood stained, serous in early case, later turbid.

5. Rheumatoid factor is usually positive.
6. Nodules usually present in the lung.
7. Systemic features are more.
8. Pleural fluid study:
 - Exudative (high protein) and glucose is low (glucose is unable to enter into pleural space, thus block entrance).
 - High cholesterol (fluid looks turbid), with high LDH, low C3 and C4 .
 - Rheumatoid factor in pleural fluid may be positive.
 - Cytology of elongated macrophage, giant multinucleated macrophage and few mesothelial cells may be present.

Characteristics of tuberculous pleural effusion

- Straw or amber colour.
- Exudative.
- High lymphocyte in pleural fluid.
- AFB is found in 20% cases.
- Culture for AFB is found in one-third cases.
- Pleural biopsy is positive in 80% cases.

Q: What are the causes of **low pH and low glucose** in pleural fluid?

A: As follows:
- Infection (empyema).
- Tuberculosis.
- Advanced malignancy.
- SLE.
- Rheumatoid arthritis.
- Oesophageal rupture.

Q: How to **treat** pleural effusion?

A: Treatment should be according to cause. For example:
- If tuberculosis: Full-course antitubercular therapy. Prednisolone 20–30 mg daily may be given for 4–6 weeks, especially in large effusion.
- If parapneumonic: Aspiration of fluid; may be repeated if necessary. Antibiotic should be given. If complicated case, especially empyema, thoracostomy may be done. Sometimes, if all fails, thoracotomy with decortication may be necessary.
- If malignancy: Treatment given accordingly. Because of recurrent effusion, pleurodesis is necessary.

Q: How **much fluid** may be drawn at a time?

A: Usually up to 1500 ml. If more is drawn, there may be risk of re-expansion pulmonary oedema.

The mechanism is: because of the fact that due to effusion, lung is compressed and there is ischaemia to lung parenchyma and necrosis of pulmonary vessels. If more fluid is drawn, there is rapid expansion of the lung, as there is no regeneration of necrotic vessels, so more leakage of fluid causing pulmonary oedema.

Q: What is the role of **steroid** in pleural effusion?

A: Steroid is mostly given in tubercular pleural effusion. Although its role is controversial, some evidence suggests that it promotes rapid absorption of pleural fluid and gives the patient quick symptomatic relief. It also prevents pleural fibrosis and adhesion. Steroid should be used along with antitubercular therapy.

Pneumothorax

Presentation of a Case

(Supposing right sided, describe the findings in right side)

On inspection:
- Restricted movement.
- Intercostal spaces: May appear full.

On palpation:
- Trachea and apex beat shifted to the left.
- Vocal fremitus reduced in right side, but normal in left side.
- Chest expansion: Reduced on the right side.

On percussion:
- Hyperresonance, but normal in left side.

On auscultation:
- Breath sound diminished or absent, but vesicular in left side.
- Vocal resonance diminished or absent, but normal in left side.

My diagnosis is **right-sided pneumothorax.**

Q: What are the **differential** diagnoses?

A: Giant bullae and big pulmonary cavity.

Q: What are the **definitive signs** of pneumothorax?

A: Hyperresonance on percussion and diminished or absent breath sound.

Q: What is **pneumothorax**?

A: Pneumothorax means presence of air in the pleural cavity.

Q: What is the **usual presentation** of pneumothorax?

A: The patient usually presents with sudden onset of unilateral pleuritic chest pain, breathlessness.

Q: Mention **one** investigation for your diagnosis.

A: X-ray chest P/A view.

Q: What **investigations** do you suggest?

A: As follows:

- Complete blood count and ESR.
- Chest X-ray P/A view.
- Sometimes, CT scan of chest.

Q: What are the **types** of pneumothorax?

A: As follows:

1. Spontaneous: It may be primary and secondary.
2. Traumatic.

Q: What are the **causes** of pneumothorax?

A: As follows:

1. Spontaneous:
 a. Primary: Without underlying lung disease. It is due to—
 - Rupture of apical subpleural bleb due to congenital defect in connective tissue of alveolar walls. Common in young, 15–30 years of age. M:F ratio is 4:1. Patient is tall, lean and thin; there is 25% chance of recurrence.
 - Rupture of emphysematous bullae or pulmonary end of pleural adhesion.

 b. Secondary: Occurs in pre-existing lung disease. Causes are—
 - Commonly COPD and tuberculosis.
 - Others: Lung abscess, acute severe asthma, bronchial carcinoma, pulmonary infarction, all forms of fibrotic and cystic lung disease, Marfan syndrome, Ehlers–Danlos syndrome and eosinophilic granuloma.
2. Traumatic:
 a. Iatrogenic: During aspiration of pleural fluid, thoracic surgery, lung biopsy or pleural biopsy, positive pressure ventilation, thoracocentesis and subclavian vein catheterization.
 b. Chest wall injury.

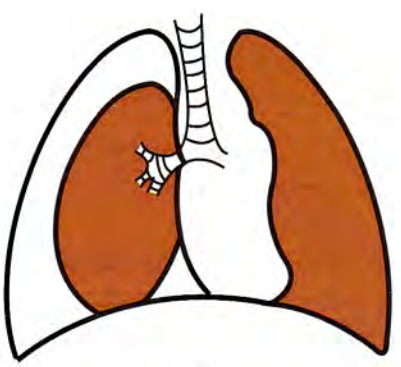
N.B. Remember the following points:

- In young patient, common cause is rupture of subpleural bleb.
- In patient >40 years of age, common cause is chronic bronchitis with emphysema.

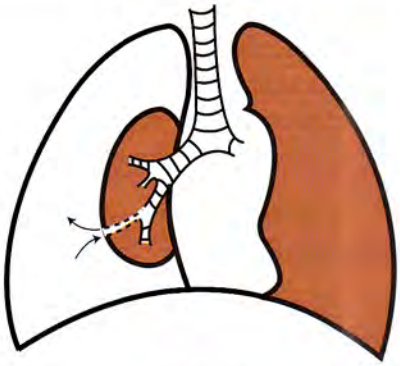
Q: What are the **types** of spontaneous pneumothorax?

A: Three types (anatomical):

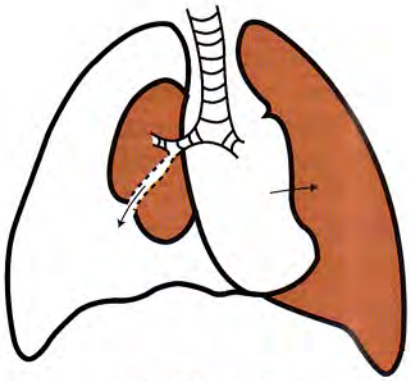
1. Closed: Communication between the lung and pleural space is sealed off. Intrapleural pressure < atmospheric pressure. Trapped air is slowly reabsorbed; lung re-expands in 2–4 weeks. Closed pneumothorax may be mild, moderate and large.
2. Open: Communication between the lung and pleural space persists (bronchopleural fistula). Intrapleural pressure and atmospheric pressure are equal throughout the respiratory cycle, which prevents re-expansion of the collapsed lung. Hydropneumothorax develops. Infection is common and empyema develops. Physical examination shows features of hydropneumothorax. Causes are—
 - Rupture of emphysematous bullae
 - Small pleural bleb
 - Tuberculous cavity
 - Lung abscess into pleural cavity.
3. Valvular: There is a communication between the pleura and the lung, which acts as a one-way valve allowing air to enter into the pleural space during inspiration, but does not let air escape on expiration. Intrapleural pressure becomes greater than the atmospheric pressure. It results in compression of the lung, shifting of mediastinum to the opposite side, compression of heart and the opposite lung also. It reduces the venous return by compressing the SVC. There is rapidly progressing breathlessness, cyanosis, shock, etc. It is a medical emergency; death may occur within minutes.



Closed type



Open type



Valvular type

N.B. Normal intrapleural pressure is negative (subatmospheric), usually −2.5 to −6.0 mmHg.

Q: How would you **grade** pneumothorax?

A: According to British Thoracic Society:

- Mild: Small rim of air around the lung, <20% of the radiographic volume.
- Moderate: Lung collapse, >20–50% of the radiographic volume.
- Large: Lung collapse, >50% of the radiographic volume.
- Tension: Pneumothorax with cardiorespiratory distress; features of shock.

Q: What are the **causes of recurrent pneumothorax** (more than twice)? How to **treat?**

A: Causes are:

- Apical subpleural bleb or cyst (congenital).
- Emphysematous bullae.
- Cystic fibrosis.
- Others: Marfan syndrome, catamenial pneumothorax, Ehlers–Danlos syndrome, α_1-antitrypsin deficiency and histiocytosis X, honey comb lung.

Treatment:

1. Chemical pleurodesis. Done by injecting tetracycline (500 mg), kaolin or talc into the pleural cavity through intercostal tube.
2. Surgical pleurodesis. Done by parietal pleurectomy or pleural abrasion during thoracotomy or thoracoscopy. Indications are:
 - All patients after a second pneumothorax.
 - Considered after first episode of secondary pneumothorax, if there is low respiratory reserve.
 - Patient who plan to continue activity, where pneumothorax would be particularly dangerous (e.g. flying or diving) should undergo definitive treatment after first episode of primary spontaneous pneumothorax.

N.B. Pleurodesis is avoided in patient with cystic fibrosis, as lung transplantation may be required and pleurodesis may make this condition technically not feasible.

Q: What are the indications of **surgery (open thoracotomy)?**

A: As follows:

- Failure of the lung to re-expand after 5 days of tube thoracotomy.
- Recurrence (usually on third recurrence).
- Bilateral pneumothorax.

Q: What is **catamenial pneumothorax?**

A: If pneumothorax develops at the time of menstruation, it is called catamenial pneumothorax. It is usually on the right side, occurs within 48 h of onset of menstruation, common in 25–30-year-old female and is due to intrapleural endometriosis.

It is **treated** by hormone therapy to suppress ovulation (by progesterone or androgen therapy) or simply by oral contraceptive pills. Sometimes, surgical exploration and pleurodesis may be needed.

Q: What is **tension pneumothorax?** What are the **causes?** How to **treat?**

A: It is a valvular type pneumothorax in which there is a communication between lung and pleural cavity with one-way valve, which allows air to enter during inspiration and prevents to leave during expiration. It causes shifting of mediastinum to the opposite side, compresses opposite lung and heart (pressure in pleural space is positive and rises above atmospheric level).

Features of tension pneumothorax:

- Severe chest pain (pain is worse with cough and relieves on sitting position).
- Severe and progressively increasing dyspnoea.
- Cough.
- Tachypnoea, tachycardia, pulsus paradoxus.
- Features of shock (hypotension, central cyanosis and tachycardia).
- Raised JVP, engorged neck vein due to compression of the heart.
- Shifting of mediastinum.

N.B. Cardinal features are progressively increasing dyspnoea and features of shock.

Causes of tension pneumothorax:

- Traumatic.
- Mechanical ventilation at high pressure.
- Rarely, spontaneous pneumothorax.

Treatment:

- Immediate insertion of wide-bore needle in second intercostal space in midclavicular line, with the patient in sitting position.
- Intrathoracic tube is inserted in fourth, fifth or sixth intercostal space in midaxillary line; and the tip of the tube should be advanced in apical direction. It is connected to an underwater seal or one-way Heimlich valve.
- Patient should be kept propped up with oxygen inhalation.
- Morphine 5–10 mg subcutaneously.
- If bubbling ceases, repeat chest X-ray. If the lung re-expands, tube may be removed after 24 h. Tube should be removed during expiration or Valsalva manoeuvre (the tube need not be clamped before removing).
- If no response or continued bubbling for 5–7 days, surgical treatment may be necessary.

Q: How do you know that the **water seal drainage** is working properly or not?

A: As follows:

- Bubbling of air in water.
- During expiration or coughing, more bubbling occurs.
- During inspiration, water column ascends within the tube, which remains under water.

Q: What **advice** is given to the patient with **water seal drainage**?

A: Never raise the bottle above the chest wall. The bottle must be kept below the level of thorax. The patient is also advised to inflate air pillows or balloons, which will help in the expansion of collapsed lung.

Q: How to **follow-up** a patient after chest tube insertion?

A: As follows:

- Bubbling: Whether it disappears or persists (indicates leaking).
- Blockage of the tube by clot or kinking.
- Malposition.
- Retrograde flow back into the chest.

Q: How to **treat** pneumothorax?

A: Depends on whether it is primary or secondary, open, closed or tension or presence of symptoms.

1. In primary small pneumothorax:
 - Spontaneous resolution occurs. Follow-up at 2-week interval (repeat chest X-ray).
 - Normal activity.
 - Avoid strenuous exercise.
2. In primary moderate-to-large with breathlessness: Percutaneous needle aspiration of air (2–5 L. Stop, if resistance to suction is felt or patient coughs).
3. In secondary pneumothorax: Patient with COPD, even small pneumothorax can cause respiratory failure. Hence, water seal drainage should be given.
4. Open pneumothorax: Surgery (as is due to bronchopleural fistula).
5. Tension pneumothorax (described as above).

Advise to the patient:

- Must stop smoking.
- Avoid air travel for 6 weeks after normal chest X-ray.
- Diving should be permanently avoided.

Q: If you are working at a **remote place** and a patient presents with tension pneumothorax, what measures should you take?

A: Immediately I shall insert a wide-bore needle (may be canula/venflon) in the second intercostal space in midclavicular line. This will allow the trapped air to escape (producing an audible hiss). Then I shall send the patient to the nearest hospital. (Do not remove the canula; tape it securely.)

Q: How **long** the lung takes to re-expand?

A: Air is absorbed at the rate of 1.25% of the total radiographical volume/day. Hence, if there is 50% lung collapse, it will take 40 days to expand.

Q: What are the possible causes of **failure of re-expansion** of lung?

A: As follows:

- Water seal drainage is not working properly or may be blocked.
- Presence of bronchopleural fistula.
- A major bronchus may be obstructed.
- Lung is completely fibrosed with permanent damage.



Right-sided pneumothorax



Left-sided hydropneumothorax

Q: What is **hydropneumothorax?** What are the **causes?**

A: When there is accumulation of fluid and air in pleural cavity, it is called hydropneumothorax. Its causes are:

- Iatrogenic (during aspiration of pleural fluid).
- Pulmonary TB.
- Bronchopleural fistula.
- Trauma (penetrating chest injury and thoracic surgery).
- Rupture of lung abscess.
- Oesophageal rupture.
- Erosion of bronchial carcinoma.

Q: What is the **bedside test** in hydropneumothorax?

A: Succussion splash.

Q: What are the **signs** of hydropneumothorax?

A: In lower part, signs of pleural effusion; and in upper part, signs of pneumothorax.

Q: What is the treatment of hydropneumothorax?

A: Water seal drainage and treatment of primary cause.

Q: What are the **indications** of chest tube or IT tube drainage?

A: As follows:

- Tension pneumothorax.
- Large second spontaneous pneumothorax if >50 years.
- Malignant pleural effusion.
- Empyema thoracis or complicated parapneumonic effusion.
- Hydropneumothorax.
- Traumatic haemopneumothorax.
- Postoperatively, e.g. thoracotomy, oesophagectomy, cardiothoracic surgery.

Bronchiectasis

(Most physical signs are found on the back of chest.)

Presentation of a Case

(Describe systematically, only auscultatory findings given. Findings on inspection, palpation and percussion are usually normal.)

- Breath sound is normal.
- Vocal resonance is normal in all the areas.
- Multiple coarse crepitations in right or left or both lung bases, altered by cough.

My diagnosis is **bronchiectasis** (right or left or bilateral or extensive).

Q: What are your **differential diagnoses?**

A: As follows:

- Diffuse parenchymal lung disease (DPLD) [idiopathic pulmonary fibrosis (IPF)].
- Pulmonary TB.

Q: Why it is bronchiectasis?

A: There are generalized clubbing and bilateral basal coarse crepitations altered by coughing. All are highly suggestive of bronchiectasis.

Q: What **else** do you want to examine?
A: I want to examine for clubbing.

Q: **What history** do you like to take if bronchiectasis?
A: History of cough with profuse expectoration of sputum, which is more marked in the morning after waking up from sleep.

Q: **Why not** IPF?
A: In IPF, crepitations are usually bibasilar, inspiratory (dry or 'Velcro' type in quality), unaltered by coughing. (In such case, usually there is history of persistent cough that may or may not be with profuse expectoration, progressively increasing breathlessness or exertional dyspnoea.)

Q: **Why not** pulmonary oedema?
A: In pulmonary oedema, there is no generalized clubbing. Also, in pulmonary oedema, crepitations are usually fine and present during both inspiration and expiration.

(In pulmonary oedema, there is history of orthopnoea or paroxysmal nocturnal dyspnoea (PND) or history suggestive of any cardiac disease.)

Q: What are the **causes** of basal crepitation?
A: As follows:

1. **Unilateral basal crepitation:**
 - Unilateral bronchiectasis.
 - Resolution stage of pneumonia.
 - Lung abscess.
 - Localized fibrosis of lung.
2. **Bilateral basal crepitation:**
 - Bilateral bronchiectasis.
 - Fibrosing alveolitis or ILD.
 - Pulmonary oedema.
3. **Causes of bilateral crepitation with clubbing:**
 - Bilateral bronchiectasis.
 - Fibrosing alveolitis or ILD.

Q: What is the **commonest site** of bronchiectasis?
A: Left lower lobe and lingula.

Q: What is **posttussive** crepitation? What is its **significance?**
A: Crepitation that appears after cough is called posttussive crepitation. It is usually at the apex and indicates TB.

Q: What are the **presentations** of bronchiectasis?
A: Cough with profuse expectoration of sputum, which is usually more marked in the morning after waking from sleep. Occasionally, haemoptysis and breathlessness in advance cases. Features of secondary infection may be present.

Q: What is **dry bronchiectasis** (bronchiectasis sicca)?
A: It is a type of bronchiectasis in which dry cough is associated with intermittent episodes of haemoptysis. It may be massive, even life threatening as bleeding is from bronchial vessels with systemic pressure. Common in patients with granulomatous infection, especially TB, and usually involves upper lobe.

Q: Why **haemoptysis?**
A: It is due to bronchial wall hypertrophy; hence mucosa becomes friable, sloughs out, capillary opens and bleeding occurs. Erosion of hypertrophic bronchial artery may result in massive haemoptysis.

Q: What is **bronchiectasis** and what are the **causes** of it?
A: It is the abnormal, permanent dilatation of one or more bronchi with destruction of bronchial wall proximal to the terminal bronchiole. Its causes are:

1. Congenital or hereditary:
 - Cystic fibrosis.
 - Kartagener syndrome (triad of bronchiectasis, dextrocardia, and sinusitis or frontal sinus agenesis).
 - Primary ciliary dyskinesia (including immotile ciliary syndrome).
 - Hypogammaglobulinaemia (of IgA and IgG; it causes recurrent infection and bronchiectasis).
 - Yellow nail syndrome.
 - Young syndrome (obstructive azoospermia and chronic sinopulmonary infection, thought to be due to mercury intoxication).
 - Sequestrate segment of lung.
2. Acquired:
 - In children, pneumonia complicating measles, whooping cough, primary TB and foreign body.
 - In adults, bronchial neoplasm, pulmonary TB, recurrent aspiration or suppurative pneumonia.
 - Allergic bronchopulmonary aspergillosis (causes proximal bronchiectasis).

N.B. In children, postmeasles or whooping cough are commonly associated with bronchiectasis. In adults, post-tubercular bronchiectasis is the common one.

Q: What are the **types** of bronchiectasis?

A: There are three types:

- Saccular or cystic (more severe form).
- Cylindrical.
- Fusiform.

Q: What are the **characteristics of sputum** in bronchiectasis?

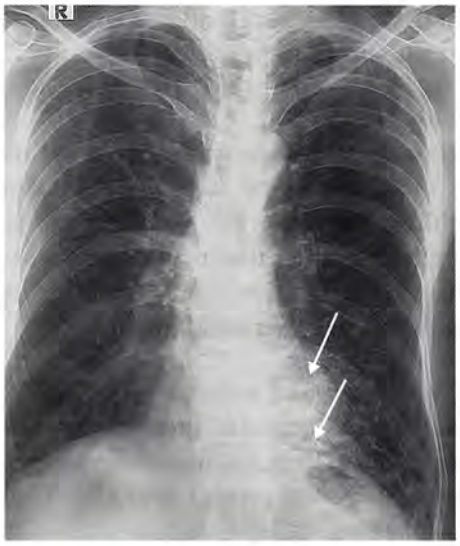
A: If the sputum is kept in a bottle, there are three layers:

- Lower sediment (epithelial debris and bacteria) layer.
- Middle thick or liquid layer.
- Upper frothy layer.

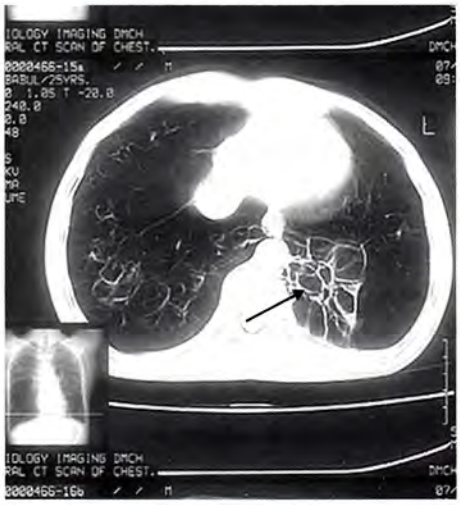
Q: What **investigations** do you suggest in bronchiectasis?

A: As follows:

1. Chest X-ray PA view (may be normal), and there may be:
 - Ring with clear centre (like honeycomb).
 - Ring with or without fluid level, may be multiple (cystic bronchiectasis).
 - Linear streaks (tram line).
 - Thick bronchi, signet ring or patchy opacity.
2. High-resolution CT scan: Definitive (preferred investigation).
3. Others:
 - Complete blood count (CBC) with ESR (may be neutrophilic leucocytosis).
 - X-ray of paranasal sinuses (PNS) (in Kartagener syndrome).
 - Lung function tests (obstructive type usually; may be restrictive in advanced case).
 - Sputum for Gram staining, C/S, AFB, malignant cell (mention if necessary according to the history).
 - Sometimes bronchoscopy to locate the site of obstruction.
 - Aspergillus precipitin antibody or skin prick test [if **allergic bronchopulmonary aspergillosis** (ABPA) is suspected].
 - Serum immunoglobulin: If hypogammaglobulinaemia is suspected (10% of adults with bronchiectasis have antibody deficiency, mainly IgA).
 - Sweat test for chloride content: If cystic fibrosis is suspected.
 - Mucociliary clearance (nasal clearance of saccharin): Normally less than 30 min. If more, it indicates ciliary dysfunction.
 - Urine for proteinuria (if amyloidosis is suspected)
 - USG of whole abdomen (if situs inversus is suspected).



Left-sided bronchiectasis



CT scan showing bronchiectasis

Q: If a patient with bronchiectasis develops **nephrotic syndrome** (or urine shows proteinuria), what is the likely diagnosis?

A: Amyloidosis (in amyloidosis, there may be splenomegaly). In longstanding bronchiectasis, amyloidosis may occur as a complication.

Q: What is the **role of CT scan** in diagnosis of bronchiectasis?

A: Conventional CT has sensitivity of 60–80%, whereas high resolution CT scan has a sensitivity of more than 90% (previously bronchography was done).

Q: What is the **difference** between standard CT scan and high-resolution computed tomography (HRCT)?

A: In standard CT, the resolution is 10-mm thick. But in HRCT, resolution is 1–2-mm thick.

Q: What are the **complications** of bronchiectasis?

A: As follows:

- Secondary infection (pneumonia and pleurisy), common organisms are *Staphylococcus aureus, Haemophilus influenzae* and *Pseudomonas aeruginosa*.
- Lung abscess.
- Pleural effusion, empyema or pneumothorax.
- Pulmonary hypertension and cor pulmonale.
- Respiratory failure.
- Amyloidosis (commonly involving spleen or kidney) in longstanding case.
- Brain abscess (metastatic cerebral abscess).
- Aspergiloma in the bronchiectatic cavity.

Q: How will you **treat** bronchiectasis?

A: As follows:

- Postural drainage, keeping the affected part remaining up and percussion over it. It is done for 5–10 min, once or twice daily.
- Antibiotic, if infection.
- Chest physiotherapy.
- Surgery (lobectomy).
- Bronchodilator drugs. Also, nebulized salbutamol may be used in asthma, COPD, cystic fibrosis and ABPA.
- Inhaled or oral steroid can decrease the rate of progression. Also, helpful in ABPA.
- In bilateral extensive bronchiectasis, lung transplantation is required.

Indications of surgery:

Usually in young patient. Indications are—

- Unilateral and localized to a single lobe or segment.
- Severe and recurrent haemoptysis.

Bronchiectasis with Cystic Fibrosis

Presentation of a Case

- Patient is young with features of bronchiectasis (see in bronchiectasis).

My diagnosis is **bronchiectasis.**

Q: What do you think the **cause** is in this young patient?

A: I want to take the history. It may be pneumonia complicating measles or whooping cough in childhood. Also, it may be due to cystic fibrosis.

Q: **Why** cystic fibrosis?

A: Because there is bilateral extensive bronchiectasis involving both lungs. It is also associated with generalized clubbing.

Q: What is **cystic fibrosis**?

A: Cystic fibrosis is a life-threatening autosomal recessive disease characterized by abnormal transport of chloride and sodium ions across an epithelium causing thick, viscous secretions and leading to bronchopulmonary infection and pancreatic insufficiency.

There is an abnormality in the gene encoding a chloride ion channel in the nasal epithelium, lungs, salivary glands, pancreas, intestine and bile ducts.

Prevalence is 1/2500.

Q: What are the **clinical features** of cystic fibrosis?

A: As follows:

1. Neonate: Failure to thrive, meconium ileus, rectal prolapse.
2. Children and young adult:
 - Respiratory: Cough, wheeze, recurrent infection, bronchiectasis, lung abscess, pneumothorax, lobar collapse, haemoptysis, respiratory failure, cor pulmonale, asthma, otitis media, sinusitis, nasal polyps, etc.
 - Abdominal: Diabetes mellitus, steatorrhoea, malabsorption, cholesterol gallstone, secondary biliary cirrhosis and portal hypertension, distal intestinal obstruction syndrome (meconium ileus equivalent syndrome). There is increased incidence of peptic ulceration and gastrointestinal malignancy.
 - Others: Male infertility (due to failure of development of vas deferens and epididymis), delayed puberty and skeletal maturity, arthritis, osteoporosis, vasculitis, hypertrophic pulmonary osteoarthropathy, clubbing, stress incontinence due to repeated forced cough. About 20% of female with cystic fibrosis are infertile.

Q: What is **distal intestinal obstruction syndrome** (meconium ileus equivalent syndrome)?

A: It is a form of small intestinal obstruction occurring during infancy and onwards in a patient with

cystic fibrosis, resulting from a combination of steatorrhea and viscid intestinal secretions, causing faecal impaction in ascending colon or in ileocaecal junction.

Q: How to **diagnose** a case of cystic fibrosis?

A: It is based on clinical history and:

- Family history of cystic fibrosis.
- Sweat test: High sweat sodium and chloride concentration over 60 mmol/L.
- Blood DNA analysis of gene defect.
- Radiological features of bronchiectasis.
- Absent vas deferens and epididymis.
- Blood immunoreactive trypsin levels (for screening purpose).

Q: What **investigations** should be done in a patient with cystic fibrosis?

A: As follows:

- Blood: CBC, liver function tests, creatinine, electrolyte, coagulation study.
- Vitamin A, D, E levels.
- Glucose tolerance test (annually).
- Bacteriology: Cough swab, sputum culture.
- X-ray chest (hyperinflation, bronchiectasis).
- USG of whole abdomen (fatty liver, cirrhosis, chronic pancreatitis)
- Spirometry (obstructive defect)
- Aspergillus serology or skin test
- Faecal fat analysis.



Bilateral bronchiectasis



Bilateral bronchiectasis in cystic fibrosis

Q: How to **treat** cystic fibrosis?

A: As follows:

1. General care:
 - Nutritional support.
 - Fat-soluble vitamin supplement.
 - Strict glucose control.
 - Smoking cessation.
 - Vaccination with influenza and pneumococcal vaccines
2. For respiratory problems:
 - Regular physiotherapy (postural drainage, active cycle techniques, forced expiratory techniques, etc.).
 - Antibiotic for acute infective exacerbations (oral or IV) and prophylactically (oral flucloxacillin or nebulized colomycin or tobramycin).
 - Symptomatic relief by mucolytic, bronchodilators, inhaled corticosteroid. In some patients, inhalation of recombinant DNAse or hypertonic saline may give some relief.
 - Oxygen therapy, as needed.
 - Pulmonary rehabilitation.
3. For advanced lung disease: Oxygen, diuretics (for cor pulmonale), noninvasive ventilation, lung or heart–lung transplantation.
4. For abdominal problems:
 - Pancreatic enzyme replacement.
 - If acute abdomen due to intestinal obstruction: Nothing by mouth, IV fluid and nasogastric

suction should be given. Acetylcysteine given intravenously or through the nasogastric tube has been shown to be useful in resolving bowel obstruction.

- Ursodeoxycholic acid for impaired liver function
- Liver transplantation may be ultimately needed in cirrhosis.

5. Others: Treatment for osteoporosis, arthritis, sinusitis, vasculitis and infertility.
6. Genetic counselling.

N.B. Remember the following points:

- Diagnosis of cystic fibrosis should be suspected in any young patient who presents with chronic respiratory and chronic gastrointestinal problem.
- Gastrointestinal problems, malabsorption and diabetes mellitus in patient with cystic fibrosis is due to pancreatic insufficiency.
- Faecal elastase is used as a screening test for exocrine pancreatic dysfunction.
- *Pseudomonas aeruginosa* is the commonest organism, causing recurrent respiratory infection.
- Prognosis: Median survival is now over 30 years.

DPLD (Previously Called Fibrosing Alveolitis or ILD)

Usual instructions are:

- Examine the back of the chest and relevant.

Presentation of a Case

1. **Inspection:**
 - The patient is dyspnoeic, hyperventilating with cyanosis (mention if present).
 - Respiratory rate is 30/min.
2. **Palpation:**
 - Trachea is central in position.
 - Apical beat is in left fifth intercostal space, just medial to the midclavicular line.
 - Chest expansion on both sides is reduced symmetrically.
 - Vocal fremitus is normal.
3. **Percussion:**
 - Percussion note is resonant over both lung fields.
4. **Auscultation:**
 - Breath sound is vesicular with prolonged expiration.
 - Bilateral basal end-inspiratory fine crepitations, unaltered by coughing, are present.
 - Vocal resonance is normal.

My diagnosis is **DPLD (fibrosing alveolitis or ILD).**

Q: What **relevants** do you like to see?

A: As follows:

- Clubbing.
- Cyanosis (usually central).
- Others to find out cause: Rheumatoid arthritis, scleroderma, dermatomyositis, SLE, history of drugs, to exclude secondary causes. See below.

N.B. Triad of clubbing, cyanosis and bilateral end-inspiratory fine crepitation is highly suggestive of DPLD.

Q: What are your **differential diagnoses?**

A: As follows:

- Bilateral bronchiectasis.
- Fibrosis of the lung due to other causes.
- Chronic heart failure (pulmonary oedema).

Q: **Why not** pulmonary oedema?

A: In pulmonary oedema, crepitations are usually fine, present during both inspiration and expiration, and are altered by coughing.

If there is clubbing, it is against pulmonary oedema. Also, in the history, there may be orthopnoea or PND or history suggestive of any cardiac disease.

Q: Why is there **end-inspiratory crepitation** in DPLD?

A: In DPLD, alveoli remain collapsed. During forceful inspiration, sudden opening of collapsed alveoli produces crepitations.

Q: What are the causes of **bilateral crepitations?**

A: As follows:

- LVF (fine crepitation, may be altered by coughing, has other evidence of LVF).
- Bilateral brochiectasis (crepitations both in inspiration and expiration, are altered by coughing).
- DPLD.

Q: What are the causes of **clubbing with bilateral basal crepitations?**

A: As follows:

- Bilateral brochiectasis.
- DPLD.
- Bronchial carcinoma.
- Bilateral extensive TB.

Q: What is **DPLD**?

A: DPLD are a heterogenous group of diseases characterized by diffuse lung injury and inflammation that can progress to lung fibrosis. Previously, it was called interstitial lung disease (ILD).

Q: **Why** is it called DPLD?

A: The term DPLD is preferred than ILD because the pathological lesion involves the alveoli along with interstitium.

Q: What **history do you like to take in** DPLD?

A: As follows:

- Onset of the disease: Acute or chronic.
- History of connective tissue disease like rheumatoid arthritis, scleroderma, dermatomyositis, SLE.
- History of drugs.
- Occupational and environmental history.

Q: What are the **presentations** with IPF?

A: Patient is usually elderly, uncommon <50 years.

- Cough, usually dry.
- Progressive breathlessness, usually exertional.
- Arthralgia, cyanosis and finger clubbing (20–50% cases).

Q: **Classify** DPLD.

A: DPLD is classified into six groups:

1. Granulomatous DPLD (e.g. sarcoidosis).
2. Granulomatous DPLD with vasculitis (e.g. Wegener granulomatosis, Churg–Strauss syndrome, microscopic vasculitis).
3. Idiopathic interstitial pneumonia (IIP):
 a. Idiopathic pulmonary fibrosis [IPF, also called usual interstitial pneumonia (UIP). It was previously called cryptogenic fibrosing alveolitis 90%].
 b. Idiopathic interstitial pneumonia other than IPF (10%):
 - Desquamated interstitial pneumonia.
 - Acute interstitial pneumonia.
 - Nonspecific interstitial pneumonia.
 - Respiratory bronchiolitis.
 - Cryptogenic organizing pneumonia [(COP, also called bronchiolitis obliterans organizing pneumonia (BOOP)].
 - Lymphocytic interstitial pneumonia.
4. Pulmonary autoimmune rheumatic diseases (e.g. rheumatoid arthritis, SLE).
5. Drugs (busulfan, bleomycin, methotrexate, nitrofurantoin, amiodarone).
6. Other forms of DPLD, e.g. histiocytosis X (Langerhans cell histiocytosis), Goodpasture syndrome, idiopathic pulmonary haemosiderosis, diffuse alveolar haemorrhage, lymphangioleiomyomatosis, pulmonary alveolar proteinosis.

Q: What **investigations** should be done in IPF?

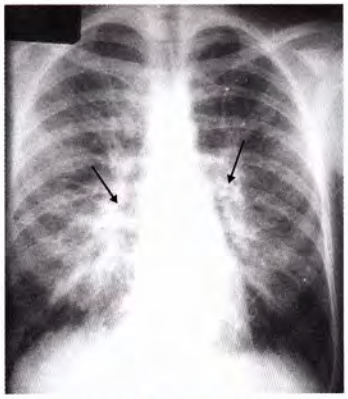
A: As follows:

1. Full blood count (shows different changes in different diseases):
 - ESR may be high (polycythaemia is rare).
 - Lymphopaenia (in sarcoidosis).
 - Eosinophilia (in pulmonary eosinophilia and drug reactions).
 - Neutrophilia (in hypersensitivity pneumonitis).
2. X-ray chest: Initially ground glass appearance, bilateral reticulonodular shadow mainly in lower zone. Lung size may be reduced; diaphragm may be raised. In advanced stage, there may be a honeycomb appearance.
3. HRCT: Helpful in early diagnosis, even when chest X-ray is normal. Changes are usually bilateral, peripheral and mainly in the lower lobes. There is patchy subpleural reticular abnormality with minimal or no ground glass changes, honeycomb (thick-walled cysts of 0.5–2 cm in terminal and respiratory bronchioles) and traction bronchiectasis.
4. Pulmonary function tests:
 - Restrictive pattern (FVC and FEV_1 are proportionately low, and ratio is normal or high).
 - Lung volumes are reduced (may be paradoxically preserved in patient with concomitant emphysema).
 - Reduced carbon monoxide (CO) transfer.
 - Peak flow rate may be normal.
5. Arterial blood gas: Hypoxaemia with normal or low P_aCO_2 (due to hyperventilation).
6. Bronchoscopy: Bronchoalveolar lavage shows increased number of cells, particularly neutrophils and macrophages. There may be increased lymphocytes in sarcoidosis, extrinsic allergic alveolitis and drug-induced lung disease. Transbronchial lung biopsy may be needed for confirmation.
7. Others (according to suspicion of cause):
 - C-reactive protein (CRP) may be raised.
 - LDH (high level indicates disease activity in DPLD).
 - For sarcoidosis: Calcium may be elevated. Urinary calcium excretion and liver biopsy may

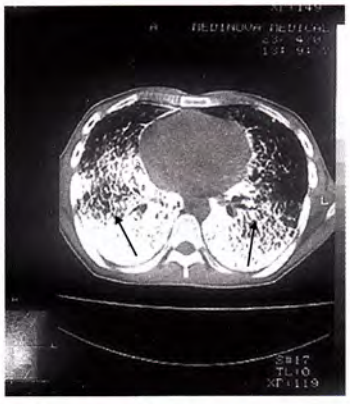
be useful. Serum ACE is an indicator of disease activity. Gallium scanning may be done.

- For autoimmune diseases: Rheumatoid factor and **anti-cyclic citrullinated peptide** (anti-CCP) antibodies. Rheumatoid arthritis (RA) test and antinuclear antibodies (ANA) are positive in 30% cases (in low titre).
- Hypergammaglobulinaemia.

8. For confirmation, lung biopsy is the definitive investigation. It is done in selected cases, if diagnosis is uncertain. Biopsy is done in the following methods:
 - Transbronchial biopsy.
 - Video-assisted thoracoscopic (VATS) lung biopsy.
 - Open lung biopsy in some cases.



Fibrosing alveolitis (DPLD)



CT scan showing fibrosing alveolitis (DPLD)

N.B. Lung biopsy is not a routine investigation. Typical clinical features and HRCT are sufficient for diagnosis. However, lung biopsy is strongly indicated in young patient.

Q: What is the **treatment** of IPF?

A: As follows:

1. Prednisolone 0.5 mg/kg with azathioprine 2–3 mg/kg is recommended in:
 - Highly symptomatic.
 - Rapidly progressive disease.
 - Ground glass opacity on CT scan.
 - Sustained >50% fall of forced vital capacity (FVC) over 3–6 month period.
2. Antifibrotic therapy (on trial):
 - Interferon-γ-1b.
 - Pirfenidone.
 - Sildenafil.
 - Bosentan.
 - Etanercept (biological agent).
 - Thalidomide.
 - *N*-acetyl cysteine.
3. Single lung transplantation in young patient at advanced stage. Survival is 1 year in 60% cases.

Prednisolone is given for at least 2 months and then tapered to a maintenance dose of 10–12.5 mg daily.

Q: What is the **prognosis** of IPF?

A: Usually 3–5-year survival in 50% cases (65% in steroid responder and 25% in steroid non-responder).

Q: What are the **complications** of IPF?

A: As follows:

- Pulmonary hypertension and cor pulmonale.
- Respiratory failure.
- Others include infection and bronchial carcinoma.

Consolidation

Presentation of a Case

(Supposing right sided, mention all findings in right side):

On inspection:

- Restricted movement.

On palpation:

- Trachea: Central and apex beat in normal position.
- Vocal fremitus is increased.

On percussion:

- There is dullness (woody), and mention the location

On auscultation:
- Breath sound is bronchial.
- Vocal resonance is increased and there is whispering pectoriloquy.
- There is (mention, if any) few crepitations or pleural rub.

My diagnosis is **right-sided consolidation**.

Q: What are the **differential diagnoses**?

A: As follows:
- Lung abscess
- Bronchiectasis.

Q: **Why not** lung abscess?

A: In case of lung abscess, auscultation will show coarse crepitations. Also, there may be combined features of cavitation and consolidation. Clubbing may be present.

(In the history, there will be profuse foul-smelling sputum. X-ray will show cavity with air–fluid level).

Q: Can it be **tuberculosis**?

A: In tuberculosis, usually there is no sign of consolidation.

(Moreover, in the history, there will be low-grade continued fever with evening rise, weight loss, anorexia, night sweat, etc.)

Q: Why not **bronchiectasis**?

A: In bronchiectasis, usually there is no sign of consolidation. Auscultation will show coarse crepitations, which are reduced or disappear on coughing. Clubbing may be present.

(In the history, there is profuse sputum production, more marked in the morning after waking from sleep.)

Q: What is the typical character of **sputum** in consolidation?

A: The sputum is usually rusty.

Q: Is there any **crepitation** in consolidation? Why?

A: Crepitation may be present during resolution of pneumonia.

Q: What **investigations** should be done in consolidation?

A: As follows:
1. Hb%, TC, DC, ESR:
 - In bacterial pneumonia: Polymorphonuclear leucocytosis.
 - In atypical pneumonia: Normal or slightly increased leucocytes.
 - In viral pneumonia: leucopaenia.
2. X-ray chest: Homogenous opacity with air bronchogram (usually found after 12–18 h). If it is associated with hilar adenopathy, then it is suggestive of *Mycoplasma pneumoniae*.
3. Sputum: Gram staining, C/S (aerobic and anaerobic).
4. Blood C/S (positive in pneumococcal pneumonia).
5. Arterial blood gas analysis.
6. Others (according to aetiology):
 - Pneumococcal antigen in serum.
 - Mycoplasma antibody detection [agglutination, complement fixation test (CFT)], Coombs test, C/S in special media.
 - Antibody against virus, *Chlamydia, Legionella*.
 - Urinary *Legionella pneumophila* antigen.
 - CRP (high).





Right-sided consolidation

N.B. Chest X-ray may reveal complications, such as pleural effusion. Also there may be cavitation (found in infection by *Staphylococcus aureus* and pneumococcal serotype 3).

Q: What is **consolidation?**

A: It means pneumonia, which is defined as inflammation in the lung parenchyma characterized by accumulation of secretion and inflammatory cells in alveoli.

Q: What are the **types** of pneumonia?

A: As follows:

1. **Anatomically of two types:**
 - Lobar: Commonly involves one or more lobe.
 - Lobular (bronchopneumonia): It is characterized by nonpatchy alveolar opacity with bronchial and bronchiolar inflammation. Commonly involves both lower lobes.
2. **Clinically of four types:**
 - Community acquired pneumonia (CAP).
 - Nosocomial (hospital acquired).
 - Pneumonia in immunocompromised.
 - Suppurative and aspiration pneumonia.

Q: What are the **presentations** of lobar pneumonia?

A: The patient may present with:

- Fever, may be with chill and rigor.
- Cough, initially short, painful and dry. Later on, expectoration (during resolution). Rusty sputum (due to *Streptococcus pneumoniae*).
- May be haemoptysis.
- Chest pain, pleuritic (may radiate to shoulder or abdomen).
- Other features: Dyspnoea, anorexia, nausea and vomiting.

Q: What are the **precipitating factors** of pneumonia?

A: As follows:

- Streptococcus pneumonia often follows viral infection with influenza or parainfluenza virus.
- Hospitalized ill patient.
- Smoking.
- Alcohol excess.
- Bronchiectasis (e.g. in cystic fibrosis).
- Bronchial obstruction.
- Immunosuppression.
- IV drug abuser.
- Inhalation from oesophageal obstruction.

Q: What are the **pathological stages** of CAP?

A: Four stages:

- Stage of congestion: Persists for 1–2 days.
- Stage of red hepatization (red and solid-like liver): Persists for 2–4 days.
- Stage of grey hepatization: Persists for 4–8 days.
- Stage of resolution: 8–9 days or more.

Q: What are the causes of **community acquired pneumonia (CAP)?**

A: It is caused by:

- Common organism: *Streptococcus pneumoniae* (50%), *Mycoplasma pneumoniae, Chlamydia pneumoniae* and *Legionella pneumophila.*
- Others: *Staphylococcus aureus, Haemophilus influenzae, Chlamydia psittaci, Coxiella burnetii* (Q fever), Klebsiella, *Actinomyses israelii* and viral (influenza, parainfluenza, measles, respiratory syncytial virus in infancy and varicella) infections.

Q: What are the **complications** of pneumonia?

A: As follows:

- Pulmonary: Lung abscess, pleurisy, pleural effusion, empyema thoracis, pneumothorax by *S. aureus*, fibrosis of lung, collapse, adult respiratory distress syndrome (ARDS), delayed or slow resolution.
- Cardiovascular: Pericarditis, myocarditis, endocarditis, arrhythmia, thromboembolic disease and peripheral circulatory failure.
- Neurological: Meningism, meningoencephalitis.
- Musculoskeletal: Septic arthritis.
- GIT: Meteorism (gaseous distension of stomach, intestine or abdomen).
- Others: Septicaemia, renal failure, hepatitis, ectopic abscess formation by *S. aureus.*

Q: What are the causes of **slow or delayed resolution** of pneumonia?

A: Delayed resolution means when the physical signs persist for more than 2 weeks and radiological features persist for more than 4 weeks after antibiotic therapy. Causes are:

- Incorrect microbiological diagnosis.
- Fungal, tubercular or atypical pneumonia.
- Improper antibiotic or insufficient dose.
- Bronchial obstruction (bronchial carcinoma, adenoma, foreign body).
- Empyema or atelectasis.
- Immunocompromised patient [HIV, diabetes mellitus (DM), lymphoma, leukaemia, multiple myeloma].

Q: What are the causes of **recurrent pneumonia** (three or more separate attacks)?

A: As follows:

- Bronchial obstruction (bronchial carcinoma, adenoma, foreign body).

- Lung disease (bronchiectasis, lung abscess, cystic fibrosis, sequestrate segment of lung: Commonly left lower lobe).
- Aspiration (achalasia cardia, scleroderma, pharyngeal pouch).
- Immunocompromised patient (HIV, DM, lymphoma, leukaemia, multiple myeloma).

N.B. Remember the following points:

- CAP usually spreads by droplet infection and most cases occur in previously healthy individual.
- Physical signs of consolidation usually appear within 2 days, and disappear within 2 weeks with proper treatment.
- Radiological opacity appears within 12–18 h, and disappears within 4 weeks with proper treatment.
- If radiological opacity persists after 8 weeks (with treatment), it is called nonresolution.

Q: What are the **criteria of assessment** of severity of CAP?

A: **CURB-65** criteria may be used for the assessment of severity of CAP. One point is scored for each of the following features:

- **C**onfusion (mini mental score 8 or less or new disorientation in person, place or time).
- **U**rea >7 mmol/L or >20 mg/dl.
- **R**espiratory rate >30/min.
- **B**lood pressure (systolic BP <90 mmHg and diastolic BP <60 mmHg).
- Age **>65** years.

This score is used for management:

- Score 0 or 1: Home treatment.
- Score 2: Hospitalization.
- Score 3 or more: Manage in hospital, may require ICU.

Other markers of severity of pneumonia:

- Chest X-ray: More than one lobe involved.
- PaO_2 <8 kPa.
- Low albumin (<35 g/L).
- White cell count (<4000/cmm or >20,000/cmm).
- Blood culture positive.

Q: What are the indications for referral for **ITU?**

A: As follows:

- CURB score 4–5.
- Persistent hypoxia despite high concentration of oxygen (PO_2 <8 kPa or 60 mmHg).
- Progressive hypercapnoea.
- Severe acidosis.
- Shock.
- Depressed consciousness.

Q: What is **nosocomial pneumonia?** What are the **causes** and **predisposing factors**?

A: New episode of pneumonia occurring at least 2 days after admission in the hospital is called nosocomial pneumonia.

Causes are: If it occurs within 4–5 days of admission (early onset), organisms are similar to CAP. However, if it occurs later (late onset), common organisms are—

- Gram-negative Enterobacteriaceae *(Escherichia coli, Klebsiella* and *Pseudomonas aeruginosa)* are common.
- *S. aureus* including methicillin resistant *S. aureus* (MRSA).
- Anaerobic organism.

Predisposing factors for nosocomial pneumonia:

- Elderly patient.
- Bed bound, unconscious [e.g. cerebrovascular accident (CVA)].
- Postoperative case (thoracic or abdominal surgery).
- Malignancy.
- Diabetes mellitus.
- Use of steroid, cytotoxic drugs, antibiotics.
- Prolonged anaesthesia, intubation, tracheostomy, IV canula.
- Achalasia of cardia, dysphagia due to any cause, vomiting.
- Bulbar or vocal cord palsy.
- Nasogastric intubation.
- Abdominal sepsis, infected emboli.

Q: How to **diagnose** nosocomial pneumonia?

A: After admission in the hospital, associated with predisposing factors, if the patient develops purulent sputum, fever associated with radiological infiltrate, leucocytosis or leucopaenia unexplained increase in oxygen requirement.

Q: How to **treat** nosocomial pneumonia?

A: Empirical antibiotic therapy should be started intravenously. It should cover Gram-negative organisms:

- A third-generation cephalosporin (e.g. cefotaxime) with an aminoglycoside (gentamicin) *or*
- Meropenem *or*
- A monocyclic β-lactam (e.g. aztreonam) and flucloxacillin.
- If MRSA is suspected, it is treated with IV vancomycin. When possible, oral therapy may be considered with doxycycline, rifampicin or linezolid.

- If pseudomonas infection is suspected, IV ciprofloxacin or ceftazidime or doripenem should be given.
- Physiotherapy and oxygen, fluid and nutritional support should be given.

N.B. Aspiration pneumonia is also common in hospital and involves multiple organisms with anaerobe. Treatment: IV Co-amoxiclav or cefuroxime plus metronidazole.

Q: What is **bronchopneumonia**?

A: It is defined as wide spread diffuse patchy alveolar opacity associated with bronchial and bronchiolar inflammation, often affecting both lower lobes. In children, it occurs as a complication of measles or whooping cough; and in elderly, a complication following bronchitis or influenza.

Q: What is **typical pneumonia?**

A: Typical pneumonia is characterized by high temperature with cough, pleuritic chest pain, features of consolidation, caused by *S. pneumoniae, S. aureus,* etc. Respiratory symptoms are more with constitutional symptoms.

Q: What is **atypical pneumonia**?

A: When pneumonia is caused by *Mycoplasma, Legionella,* Coxiella, Chlamydia. In these cases, constitutional symptoms are more than respiratory symptoms. Features are:

- Gradual onset.
- Dry cough.
- Low-grade fever.
- Constitutional symptoms are more than respiratory symptoms (headache, myalgia, fatigue, nausea, vomiting).
- Less physical finding in the chest.

N.B. However, the term atypical pneumonia is abandoned.

Q: How to **diagnose and treat** *Mycoplasma pneumoniae?*

A: It is common in children and young adults, and is usually associated with headache, malaise and severe cough. Physical signs are less marked. Epidemics occur in cycle every 3–4 years.

Investigations:

- WBC (normal).
- Chest X-ray (commonly lower lobe involvement), may show bilateral patchy consolidation.
- Cold agglutinin (positive in 50% cases).
- Rising antibody titre [compliment fixation tests (CFT)] for *Mycoplasma pneumoniae.*
- Others (CFT and haemagglutination test).

Extrapulmonary complications of *M. pneumoniae*:

- Maculopapular skin rash, erythema multiforme and Stevens–Johnson syndrome.
- Myocarditis and pericarditis.
- Haemolytic anaemia (Coombs test may be positive) and thrombocytopaenia.
- Meningoencephalitis, **Guillain–Barré syndrome** (GBS) and other neurological abnormalities.
- Myalgia and arthralgia.
- Gastrointestinal symptoms like vomiting, diarrhoea.

Treatment:

- Clarithromycin 500 mg twice daily orally or IV **or** erythromycin 500 mg 6 hourly orally or IV for 7–10 days.
- **Or,** doxycycline 100 mg twice daily.
- Rifampicin 600 mg 12 hourly.

Q: How to **diagnose and treat** *Legionella pneumophila?*

A: Three patterns of Legionnaires' disease may occur:

- Outbreak of infection is usually associated with contaminated water supply or cooling system, or from stagnant water in cistern or shower head.
- Sporadic case, where source is unknown. It is usually common in middle-aged and elderly, more in smokers.
- Outbreaks may occur in immunocompromised patients, e.g. those on corticosteroid therapy. Diabetes and chronic kidney disease (CKD) also increase risk.

Features are: Initially viral-like illness with high fever, chill and rigor, malaise, myalgia and headache. Initially dry cough, later productive and purulent. There may be nausea, vomiting, diarrhoea and pain abdomen. Mental confusion and other neurological signs; even coma may be present. Occasionally, renal failure and haematuria may be seen.

Investigations:

- WBC: Lymphopaenia without marked leucocytosis.
- Chest X-ray: Usually shows lobar and then multilobar shadowing. A small pleural effusion may be present. Cavitation is rare.
- Hyponatraemia.
- Hypoalbuminaemia.
- High serum aminotransferases, creatine phosphokinase.

- Direct immunofluorescent for *Legionella* in pleural fluid, sputum or bronchial washings. Culture on special media can be done, but takes 3 weeks.
- *Legionella* serology: fourfold rise is highly suggestive.
- Urine for antigen (highly specific).
- Urine R/E shows haematuria.

Treatment:

- Clarithromycin 500 mg twice daily orally or I/V or Erythromycin 500 mg 6 hourly orally or I/V for 7–10 days.
- Rifampicin 600 mg 12 hourly.

Prognosis: 10% mortality (may be up to 30% in elderly).

Q: How to **treat** pneumonia?

A: Sputum should be sent for C/S and before starting antibiotic. The treatment involves:

1. General treatment: Rest, O_2 therapy, adequate hydration and chest physiotherapy.
2. Antibiotic (empirically with suspicion of cause).

Community acquired pneumonia (CAP):

1. Mild CAP:
 - Amoxicillin 500 mg 8 hourly orally or erythromycin 500 mg 6 hourly or clarithromycin 500 mg twice daily or azithromycin 500 mg daily.
 - If *S. aureus* is suspected: Clarithromycin 500 mg twice daily orally or IV, **plus** flucloxacillin 1–2 g 6 hourly IV.
 - If *Klebsiella* is suspected: Ciprofloxacin 200 mg IV 12 hourly, **plus** gentamycin 60–80 mg IV 8 hourly (see serum creatinine level) or gentamycin plus ceftazidime 1 g IV 8 hourly.

 Duration of treatment: 7–10 days (up to 14 days).

 - If *Mycoplasma, Legionella* or atypical organism is suspected: Clarithromycin 500 mg twice daily orally or erythromycin 500 mg 6 hourly orally, or tetracycline or doxycycline may be used.

 Duration of treatment: 2–3 weeks.

2. Severe CAP:
 - Clarithromycin 500 mg twice daily IV or erythromycin 500 mg 6 hourly IV.
 - **Plus** add one of the following –
 i. Co-amoxiclav 1–2 g 8 hourly IV.
 ii. Cefuroxime 1.5 g 8 hourly IV
 iii. Ceftriaxone 1–2 g IV daily.
 iv. Amoxicillin 1 g 6 hourly IV.
 v. If *S. aureus* is suspected: Flucloxacillin 2 g 6 hourly IV or sodium fusidate is added.

Q: What are the criteria for **discharge** of a patient with pneumonia from hospital?

A: To discharge, the patient should be clinically stable with no more than one of the following clinical signs:

- Temperature >37.8 °C.
- Heart rate >100/min.
- Respiratory rate >24/min.
- Systolic BP <90 mmHg.
- SaO_2 <90%.
- Inability to maintain oral intake.
- Abnormal mental status.

Q: What are the **differences** between bacterial and viral pneumonia?

A: As follows:

Points	Bacterial pneumonia	Viral pneumonia
Onset	Abrupt	Less abrupt
History of upper respiratory tract infection	Absent	Present
Systemic features	High-grade fever with chill and rigor	Low-grade fever, headache and malaise
Cough	Initially dry, later rusty sputum or purulent	Usually dry (extrathoracic complains are more)
Pleuritic chest pain	Common	Less common (respiratory complains are less common) and constitutional symptoms predominate
Physical signs of consolidation	Well marked	Minimal
Blood count	Leucocytosis	Normal or leucopaenia
Chest X-ray	Lobar or segmental homogeneous opacity with air bronchogram	Mottling or reticular pattern or patchy opacity or streaky
Sputum culture	Organism found	No organism

Lung Abscess

Presentation of a case: (Present as in consolidation)
My diagnosis is **lung abscess.**

Q: What are the **differential diagnoses**?
A: As follows:
- Consolidation (during resolution stage).
- Bronchiectasis.

Q: Why **not** consolidation?
A: Because in lung abscess:
- The patient is toxic with high temperature.
- Clubbing is present, which is against consolidation.

Q: With these findings, can it be **consolidation** only?
A: Yes, it may be during resolution stage.

Q: Could it be **bronchiectasis?**
A: Yes, because there is clubbing with coarse crepitations. However, in bronchiectasis, crepitations are mostly on the basal area. Also, there is no fever and patient is not toxic in bronchiectasis (until there is secondary infection).

Q: What **investigations** should be done in lung abscess?
A: As follows:
- CBC (leucocytosis).
- X-ray chest (cavity with air–fluid level).
- Sputum examination: Gram staining, C/S (both aerobic and anaerobic), AFB, fungus, malignant cells.
- Bronchoscopy (to exclude mass and foreign body).
- CT or MRI (in some cases).
- Blood sugar.



Left-sided lung abscess



Multiple lung abscesses

Q: What is **lung abscess?** What are the **causes?**
A: It is a localized area of suppuration within the lung parenchyma that leads to parenchymal destruction and is manifested radiologically as a cavity with air–fluid level **(not due to TB).**

Causes of lung abscess:
- Aspiration of nasopharyngeal or oropharyngeal contents: Such as in vomiting, anaesthesia, tooth extraction, tonsillectomy, unconscious patient, alcoholism and achalasia of cardia. Organisms are aerobic and anaerobic.
- Specific infections (*S. pneumoniae* type 3, *S. aureus, K. pneumoniae* and fungal). In HIV, *Pneumocystis jiroveci, Cryptococcus neoformans* and *Rhodococcus equi.*
- Obstruction by bronchial carcinoma, adenoma and foreign body.
- Infection in pulmonary infarction (by *S. pneumoniae, S. aureus, Haemophilus influenzae* and anaerobic).
- Spread from liver abscess and subphrenic abscess (due to transdiaphragmatic spread).
- Haematogenous from other infection as septic emboli (pelvic abscess and salpingitis, right-sided endocarditis, IV drug abuse).

Q: How the patient of lung abscess usually **presents?**
A: As follows:
- Severe cough with profuse foul-smelling sputum, may be foetid (anaerobic).
- Haemoptysis.
- Chest pain (pleuritic).

- Fever, usually high with chill and rigour, with profuse sweating.
- Malaise, weakness and loss of weight.

Q: What are the **physical findings** in lung abscess?

A: It depends on site. If deep seated within the lung parenchyma, there may not be any physical findings. If it is near the surface, findings are:

- Features of consolidation, usually.
- Rarely, features of cavitation.
- Sometimes, combined features of consolidation and cavitation, if large abscess.

Q: What are the **characteristics of sputum** in lung abscess?

A: If the sputum is kept in a bottle, there are three layers (as in bronchiectasis):

- Lower: Sediment (epithelial debris and bacteria).
- Middle: Thick liquid.
- Upper: Frothy.

Q: What is the **common site** of lung abscess?

A: As follows:

1. Lung abscess is common in right middle lobe.
2. If it is due to aspiration, then the commonest site depends on the posture of the patient during aspiration.
 - If the patient is lying down, abscess forms in the posterior segment of upper lobe or superior segment of lower lobe.
 - If the patient is in upright position, the common site is basal segment.

Q: Why lung abscess is more common on the **right side**?

A: Lung abscess is more common in right side due to less obliquity of the right major bronchus.

Q: What are the **complications** of lung abscess?

A: As follows:

- Pleurisy.
- Empyema.
- Bronchiectasis.
- Fibrosis.
- Septicaemia.
- Cerebral abscess (common in parietal lobe or posterior frontal region).
- Amyloidosis (rare), in chronic cases.

Q: How to **treat** lung abscess?

A: Sputum is sent for C/S and broad-spectrum antibiotic should be started.

- Broad-spectrum antibiotic: Amoxicillin or Co-amoxiclav or erythromycin **plus** metronidazole. **Or,** cefuroxime 1 g IV 6 hourly **plus** metronidazole 500 mg IV 8 hourly for 5 days, followed by cefaclor **plus** metronidazole (in 70% cases anaerobic organisms are present, but mixed organisms are also common).
- If improves, continue as above. If no response, antibiotic is given according to C/S. Treatment should be continued for 4–6 weeks.
- Postural drainage and chest physiotherapy.
- If no response to medical therapy (occurs in 1–10% cases), percutaneous aspiration (USG or CT guided).
- Sometimes, surgery (lobectomy) may be done.
- Treatment of the cause, if present.

Indications of surgery:

- No clinical response.
- Increasing size of the abscess.
- Massive haemorrhage or haemoptysis.

Other causes of cavitary lesion in lung

- Tuberculosis.
- Cavitating bronchial carcinoma.
- Pulmonary infarction.
- Fungal infection (histoplasmosis).
- Wegener granulomatosis.
- Rheumatoid nodules.
- Consolidation (*St. pneumoniae* serotypes 3).

Q: What are the causes of **multiple cavitary lesions** in the lung?

A: As follows:

- Tuberculosis.
- Staphylococcal lung abscess (in children).
- Fungal infection.
- Klebsiella.
- Amoebiasis.

Q: What are the causes of **multiple lung abscess**?

A: As follows:

- Aspiration of infected material.
- *S. aureus* (in children).
- Klebsiella infection.
- Fungal infection.
- Amoebiasis.

Collapse of Lung

Presentation of a Case

(Supposing right sided, mention the findings in right side)

On inspection:

- Restricted movement.
- Slight flattening of upper part and crowding of ribs.

On palpation:

- Trachea: Shifted to the right.
- Apex beat: Shifted to the right (mention where).
- Vocal fremitus: Reduced or increased.

On percussion:

- Dullness in upper part of chest (mention up to ..., the position).
- Upper border of liver dullness is in the right fourth intercostal space in the midclavicular line.

On auscultation:

- Breath sound: Bronchial or reduced.
- Vocal resonance: Increased or decreased, there is whispering pectoriloquy (present, if bronchial sound is present).

My diagnosis is **right-sided lung collapse.**

Q: Could it be **fibrosis?** Or what is your **differential diagnosis?**

A: It may be fibrosis. Signs of collapse and fibrosis are almost similar. However, some findings are highly suggestive of fibrosis, as it is a chronic process:

- Flattening of chest,
- Crowding of ribs, and
- Drooping of shoulder on the affected side.

These findings may be present in collapse also, if it is prolonged. All other signs of collapse are same as in fibrosis, but with less degree. To be confirmed, chest X-ray will help, which shows:

- In collapse, the X-ray shows homogeneous opacity. Evidence of bronchial obstruction (mass lesion) may be seen, and diaphragm may be elevated.
- In fibrosis, nonhomogeneous opacity, rib crowding and ring shadow due to dilatation of bronchi within fibrosis may be seen.

N.B. Signs of collapse depend on patency of the bronchus:

- If bronchus is completely obstructed (central collapse), all the signs will be **collapsed** (absent or reduced).
- If bronchus is patent (peripheral collapse), there is bronchial sound and increased vocal resonance.

Q: Why not this is a case of **pleural effusion?**

A: In pleural effusion, trachea and apex beat are shifted to the opposite side.

Q: Why not this is a case of **thickened pleura?**

A: In thickened pleura, there is no shifting of trachea and apex beat.

Q: Why not **consolidation**?

A: In consolidation trachea and apex beat will not be shifted; percussion is woody dull.

Q: What are the **types** of collapse?

A: As follows:

a. Etiologically:

1. Compression collapse (passive): Due to pleural effusion, pneumothorax and hydropneumothorax. Trachea and apex beat are shifted to the opposite side.
2. Absorption collapse (active): Caused by bronchial obstruction due to any cause. Air is absorbed distal to the obstruction and affected part is collapsed. Causes are:
 - Neoplasm (bronchial carcinoma, adenoma).
 - Foreign body (inert object and artificial teeth).
 - Mucous plug (due to bronchial asthma, cystic fibrosis, postoperative).
 - Aspergilloma.
 - Pressure on bronchus from outside (enlarged lymph node, aortic aneurysm, pericardial effusion causing collapse of left lung and enlarged left atrium in mitral stenosis).
 - Rarely, congenital collapse due to absence of surfactant.

b. Anatomically:

1. Central: Mass lesion (shows more signs and symptoms).
2. Peripheral: Usually small collapse (shows less signs and symptoms).

Causes of collapse according to age:

- Neonate: Congenital due to low or absent surfactant, aspiration of meconium.
- Children: Foreign body.
- Young: Bronchial adenoma and foreign body.
- Elderly: Bronchial carcinoma and foreign body (artificial tooth).

Q: How can you **differentiate** central and peripheral collapse clinically?

A: As follows:

- In central collapse: Bronchus is completely obstructed. So, breath sound is diminished or absent. Vocal resonance is diminished or absent.
- In peripheral collapse: Bronchus is patent. So, breath sound is bronchial and vocal resonance is increased.

N.B. Commonest cause of collapse:

- Central: Bronchial carcinoma or adenoma, enlarged lymph node or foreign body.
- Peripheral: Mucus plugging, bronchial cast.

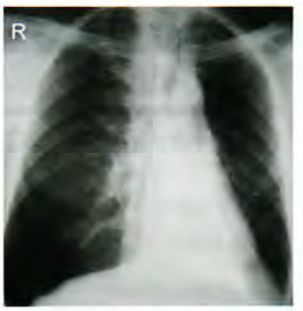
Q: What **investigations** should be done in collapse of lung?

A: As follows:

- CBC.
- Chest X-ray, PA view (homogenous opacity, heart and lung shifted to the affected side), and lateral view, if needed.
- CT scan of chest.
- Bronchoscopy (to see any obstruction, removal of foreign body, aspiration of any material, biopsy).



Right upper lobe collapse



Left lower lobe collapse



Left lung collapse

Q: What is **middle lobe syndrome?**

A: Middle lobe syndrome is the recurrent or persistent atelectasis of right middle lobe. The right middle lobe originates at acute angle and is completely surrounded by lymph nodes. It is frequently obstructed by enlarged lymph nodes due to malignancy or TB causing collapse of the lobe. There may be bronchiectatic changes. Foreign body may also be responsible.

Diagnosis:

- CT scan or MRI.
- Bronchoscopy is also helpful.

Fibrosis of Lung

Presentation of a Case

(Supposing left sided)

- There is flattening of upper part of chest, crowding of ribs, drooping of the shoulder.
- Plus, other findings as in collapse (see collapse of the lung).

My **differential diagnoses** are:

- Fibrosis of the left lung.
- Collapse of the left lung.

Q: What is the **more likely** diagnosis in this case? **Why?**

A: Fibrosis of the left lung because there is flattening of upper part of chest, crowding of ribs, drooping of the shoulder, which indicates fibrosis that is a chronic process.

Q: Can it be **collapse** also?

A: Yes, if it is longstanding or chronic.

Q: What are the **causes** of fibrosis?

A: Localized fibrosis may occur in:

- Upper lobe: TB (the commonest).
- Lower lobe: bronchiectasis (the commonest).

Causes of upper lobe (zone) fibrosis—mnemonic: SCHART

- **S:** Silicosis, sarcoidosis.
- **C:** Coal worker's pneumoconiosis.
- **H:** Histiocytosis and histoplasmosis.
- **A:** Allergic bronchopulmonary aspergillosis and ankylosing spondylitis.
- **R:** Radiation (typically in mid zone).
- **T:** TB.

Causes of lower lobe (zone) fibrosis—mnemonic: RASIO

- **R:** Rheumatoid arthritis.
- **A:** Asbestosis.
- **S:** Scleroderma.
- **I:** Idiopathic pulmonary fibrosis.
- **O:** Others (drugs: bleomycin, busulphan, nitrofurantoin, methotrexate and amiodarone).

N.B. Generalized fibrosis involving both the lungs occur in DPLD.



Bilateral apical fibrosis



Fibrosis of the left lung

Q: What are the types of fibrosis of the lung?

A: As follows:

- Focal fibrosis due to inhalation of mineral dust (pneumoconiosis).
- Replacement fibrosis (damaged lung tissue replaced by fibrosis), e.g. TB.
- Interstitial fibrosis due to any cause of DPLD (RA, systemic sclerosis or SLE).



Drooping of left shoulder with flattening of the chest

Chronic Obstructive Pulmonary Disease (COPD)

Presentation of a Case

- The patient is dyspnoeic with pursing of lips.

On inspection:

- The patient is dyspnoeic with pursing of lips, and respiratory rate is 30/min.
- The chest is barrel shaped.
- Indrawing of lower intercostal space on inspiration (due to low flat diaphragm).
- Suprasternal and supraclavicular space excavation.
- Prominent accessory muscles of respiration.

On palpation:

- Trachea, central, tracheal tug is present (descent of trachea during inspiration).
- Cricosternal distance (distance between suprasternal notch and cricoid cartilage) is reduced (normally three fingers or more).
- Apex beat is not felt.
- Chest expansion is reduced and chest movement is vertical.
- Vocal fremitus is reduced on both sides.

On percussion:

- Increased resonance or hyperresonance in both lung fields.
- Obliteration of liver and cardiac dullness (liver dullness may be lower down).

On auscultation:

- Breath sound, diminished; but vesicular with prolonged expiration.
- Few rhonchi may be present, if associated with chronic bronchitis.
- Vocal resonance normal.

My diagnosis is **COPD,** more **likely pulmonary emphysema**.

N.B. If plenty of rhonchi are present in both lung fields, then diagnosis is **chronic bronchitis with emphysema**.

Q: What is your **differential diagnosis**?
A: Chronic, severe or persistent bronchial asthma.

Q: What is the basic **difference** between bronchial asthma and COPD?
A: Bronchial asthma is reversible, but COPD is not fully reversible and is progressive.

Q: How to **confirm** COPD?
A: By spirometry and reversibility test.

Q: What are the **findings** in spirometry?
A: As follows:

- FEV_1 <80% predicted.
- FEV_1: FVC <70% predicted.
- Bronchodilator reversibility test shows <15% increase in FEV_1 after giving bronchodilator.

Q: What **investigations** should be done in COPD?
A: As follows:

1. Complete blood count (there may be polycythaemia and increased PCV due to persistent hypoxaemia).
2. Chest X-ray PA view (there may be features of hyperinflation: Increased translucency, low flat diaphragm, tubular heart, widening of intercostal space, emphysematous bullae).
3. ECG (usually normal. In cor pulmonale, there may be features of right ventricular hypertrophy (RVH).
4. Echocardiogram (may show features of cor pulmonale).
5. Lung function tests:
 - FEV_1 and FVC are reduced. Ratio of FEV_1:FVC is also reduced (indicates obstructive airway disease).
 - Postbronchodilator FEV_1 <80% of the predicted value and FEV_1/FVC is <70%.
 - Other tests: Lung volumes may be normal or increased. Gas transfer coefficient of carbon monoxide is low, when significant emphysema is present.
6. PEFR (reduced).
7. Blood gas analysis:
 - Often normal at rest.
 - PO_2 (reduced).
 - PCO_2 (normal or increased).
 - pH (acidosis).
8. High-resolution CT: Assessment of COPD, characters of emphysema, particularly bullae.
9. Sputum examination (if superadded infection).
10. α_1-antitrypsin deficiency: May be done in young, nonsmoker patient with basal emphysema.



Emphysema



Lip pursing

Q: What is COPD?

A: It is a disease characterized by airflow limitation, which is chronic, slowly progressive, and not fully reversible (bronchial asthma is reversible). It is diagnosed by history and spirometry. Postbronchodilator shows FEV_1 < 80%, predicted, and FEV_1:FVC <70%, predicted. COPD includes chronic bronchitis and emphysema.

Q: What is the **mechanism of airflow limitation** in COPD?

A: As follows:

- Increased mucus production and reduced mucociliary clearance.
- Loss of elastic recoil.
- Increased muscle tone.
- Pulmonary hyperinflation.

Q: What are the **presentations** of COPD?

A: Usually the patient is above 40 years, male and smoker. Features are:

- Chronic cough and sputum production, which is progressively increasing.
- Progressively increasing breathlessness.
- There may be haemoptysis, oedema and morning headache (due to hypercapnia).

Q: What are the **systemic features** in COPD?

A: Muscular weakness, peripheral oedema due to impaired salt and water excretion, weight loss due to altered fat metabolism, increased osteoporosis, increased circulating inflammatory markers.

Q: What are the **risk factors or causes** of COPD?

A: Multiple factors may be responsible for COPD, such as:

1. Exposure to:
 - Smoking (the commonest): Active or passive.
 - Indoor and outdoor air pollution.
 - Occupation: Exposure to dust, fumes, smokes, chemicals, etc. (e.g. coal miners and those who work with cadmium).
 - Urban dweller.
 - Low socioeconomic status.
 - Low birth weight.
 - Poor lung growth that may be due to childhood infections or maternal smoking.
 - Infections: Recurrent lung infection, persistent adenovirus in lung tissue, HIV infection is associated with emphysema.
 - Cannabis smoking (controversial).
2. Host factors:
 - Genetic factors: α_1-antitrypsin deficiency.
 - Airway hyperreactivity.
 - More in male and Caucasians.
 - Biofuel mass.

Q: What **organisms** are associated with acute exacerbation of COPD?

A: Common organisms: *Haemophilus influenzae* and *S. pneumoniae*. Other less common organisms are *Moraxella catarrhalis, Chlamydia pneumoniae* and *Pseudomonas aeruginosa*.

Q: What are the **stages or classification** of COPD?

A: According to the GOLD criteria, COPD is classified as follows:

Stage	Spirometry	Symptoms
0 – At risk	Normal	Presence of chronic symptoms (cough, sputum production)
I – Mild	FEV_1/FVC <70% $FEV_1 \geq 80\%$ predicted	None or mild
II – Moderate	FEV_1/FVC <70% $FEV_1 \geq 50\%$, but <80% predicted	Mild-to-moderate symptoms
III – Severe	FEV_1/FVC <70% $FEV_1 \geq 30\%$, but <50% predicted	Breathlessness on minimal exertion, e.g. dressing
IV – Very severe	FEV_1/FVC <70% FEV_1 <30% predicted or FEV_1 <50% predicted plus chronic respiratory failure	Breathlessness at rest

Q: What are the **complications** of COPD?

A: As follows:

- Pulmonary hypertension.
- Cor pulmonale.
- Respiratory failure.
- Secondary infection.
- Polycythaemia.

Q: How to **manage** COPD?

A: As follows:

1. Smoking must be stopped.
2. Avoidance of dust, fume, smoke, etc.
3. Drug therapy according to the stage:

I – Mild	• Avoid of risk factors, influenza vaccination • Short-acting inhaled bronchodilator like β_2 agonist (salbutamol, terbutaline) or anticholinergic (ipratropium) when needed

II – Moderate	Above treatment plus: • Regular treatment with one or more long-acting bronchodilator like β_2 agonist (e.g. salmeterol, formoterol) or anticholinergic (tiotropium) when needed • Rehabilitation
III – Severe	Above treatment plus: • Inhaled steroid (fluticasone)
IV – Very severe	Above treatment plus: • Long term oxygen, if chronic respiratory failure • Surgical treatment, if needed

4. Other therapy:
 - Oxygen, if needed.
 - Mucolytic (acetylcysteine).
 - Antibiotics (if infection).
 - Diuretic (if oedema).
 - Pulmonary rehabilitation.
 - Pneumococcal vaccination.
 - Reduction of obesity.
5. Surgical intervention:
 - Bullectomy: If young patient, large bulla compressing surrounding lung tissue, no generalized emphysema.
 - Lung volume reduction surgery (LVRS): Predominant upper lobe emphysema, preserved gas transfer and no evidence of pulmonary hypertension.
 - Lung transplantation.

Q: How **domiciliary oxygen** is given? What is the **aim** of the therapy?

A: O_2 is given 2–4 L/min for 15 h/day by nasal prongs. The aim is to increase the PaO_2 to at least 8 kPa (60 mmHg) at sea level during rest or SaO_2 to at least 90%. (Greater benefit may be seen in patients who receive > 20 h/day.)

N.B. Regarding air travel:

- Preflight assessment should be done by spirometry and a hypoxic challenge test with 15% oxygen. If saturation is maintained >90%, the patient can be allowed to travel. If not, air travel should be avoided or undertaken only with inspired oxygen therapy.
- Sufficient supplementary oxygen should be given during flight to keep the PaO_2 above 50 mmHg, which is achieved by increasing the flow by 1–2 L/min.
- Patients who use to take continuous oxygen at home will require this supplementation.

Q: What is the role of **inhaled steroid** in COPD?

A: Inhaled steroid is recommended for symptomatic patient with moderate-to-severe COPD and for patients with frequent exacerbations, but not in mild COPD. It reduces the frequency and severity of exacerbation. There is small improvement of FEV_1; but it does not alter the natural history of FEV_1 decline.

Q: What are the indications of **long-term domiciliary oxygen therapy** in COPD?

A: As follows:

1. PaO_2 <7.3 kPa (55 mmHg) irrespective of $PaCO_2$ and FEV_1 <1.5 L.
2. PaO_2 7.3–8 kPa (55–60 mmHg) associated with:
 - Pulmonary hypertension.
 - Peripheral oedema.
 - Nocturnal hypoxaemia.
 - Secondary polycythaemia.
3. Carboxyhaemoglobin <3% (in patient who have stopped smoking).
4. Terminally ill patient of whatever cause with PaO_2 <7.3 KPa.

N.B. Arterial blood gases should be measured in clinically stable patients on optimal medical therapy on at least two occasions, 3 weeks apart.

Q: **Why low concentration O_2 is given in COPD? Or what happens when high-flow O_2 is given?**

A: In COPD, the patient is dependent on hypoxic drive. Low-flow oxygen is due to its effect in the chemoresponsiveness of the respiratory centres in the medulla (part of the brainstem). High-flow oxygen blunts responsiveness of the respiratory centre in the medulla and causes carbon dioxide retention, so aggravates respiratory failure (type 2 respiratory failure).

Q: What is the role of **oral steroid** in COPD? What is the indication of steroid in COPD?

A: Oral steroid is useful during exacerbation, but maintenance therapy should be avoided.

Indications are:

- Stage III or IV disease.
- In stage II, if oral steroid trial shows responsiveness.
- Severe exacerbations of COPD.
- Frequent episodes of exacerbations.

Q: What is the role of **inhaled steroid** in COPD?

A: Inhaled steroid is recommended for symptomatic patients with moderate-to-severe COPD and for patients with frequent exacerbations; but not in

mild COPD. It reduces the frequency and severity of exacerbation. There is small improvement of FEV_1, but it does not alter the natural history of FEV_1 decline.

Q: What is the **prognosis** of COPD?

A: Prognosis of COPD is predicted by **BODE** index:

Variable	Points on BODE index 0	1	2	3
Body mass index	>21	≤21		
Obstruction to airflow (FEV_1% predicted)	≥65	50–64	36–49	≥35
Dyspnoea (MMRC scale)	0–1	2	3	4
Exercise capacity (metres walked in 6 min)	≥350	250–349	150–249	≤149

4-year mortality rate for BODE index 0–2 is 10%, whereas that of BODE index 7–10 is 80%.

N.B. Poor prognostic factors are advancing age (inversely related), fall of FEV_1 over time, weight loss and pulmonary hypertension.

Q: How to manage **acute exacerbation** of COPD (type II respiratory failure)?

A: As follows:

- Oxygen: Continuous low concentration oxygen via Venturi mask to raise PaO_2 >8 kPa (60 mmHg). Initially 24 or 28% oxygen is given and increased gradually, provided $PaCO_2$ does not rise unacceptably. If $PaCO_2$ rises and pH falls below 7.25, artificial ventilation or a respiratory stimulant should be given.
- Bronchodilator: Nebulized short-acting β_2-agonist (e.g. salbutamol) with an anticholinergic agent (e.g. ipratropium).
- Oral prednisolone 30 mg daily for 10 days.
- Antibiotic: Given if infection is suspected.
- Diuretic: If peripheral oedema.
- Chest physiotherapy. Secretions should be removed by suction.
- Respiratory support: If above treatment fails or there is tachypnoea and acidosis (pH <7.35). Noninvasive ventilatory technique like bilevel positive airway pressure (BiPAP) is used first. Continuous positive airway pressure (CPAP) is occasionally needed.
- Respiratory stimulant: Less used. Doxapram 1.5–4.0 mg/min by slow IV infusion may be helpful.

N.B. Many patients with exacerbation of COPD can be managed at home with increased bronchodilator, short course of **oral steroid** and antibiotic.

Indications of hospitalization are:

- Severe symptoms **or acute worsening that fails to** respond to outpa**tient management.**
- Presence of cya**nosis.**
- Peripheral oede**ma.**
- Alteration of con**sciousness.**
- Comorbidity and **poor social circumstances.**

Q: What are the discharge criteria of COPD patient?

A: As follows:

- The pa**tient should be in a clinically stable condition** and no **parenteral therapy should be there for 24 h.**
- Inhaled **bronchodilators are required less than** 4 ho**urly.**
- Oxygen delivery has ceased for 24 h.
- The patient is able to eat and sleep without significant episodes of dyspnoea.
- The patient or caretaker understands and is able to administer medications.
- Follow-up and home care arrangements [e.g. home oxygen, home care, Meals on Wheels, community nurse, allied health, general practitioners (GP), specialist] have been completed.
- If previously able, the patient is ambulating safely and independently, and performing activities of daily living.

Chronic Bronchitis

Presentation of a Case

Inspection:

- Shape of the chest: Normal.
- Movement of the chest: Bilaterally restricted.
- Intercostal space: Appears full.

Palpation:

- Trachea: Central.
- Apex beat: In the left fifth intercostal space in the midclavicular line.
- Chest expansion: Reduced.
- Vocal fremitus: Normal.

Percussion:

- Percussion note: Normal resonance.
- Area of liver dullness: In the right fifth intercoastal space in midclavicular line.
- Area of cardiac dullness: Impaired.

Auscultation:

- Breath sounds: Vesicular with prolonged expiration.

- Added sounds: Plenty of rhonchi, in both lung fields, present in both inspiration and expiration.
- Vocal resonance: Normal.

[**FET** (forced expiratory time): 8 s (normally, <6 s)]

My diagnosis is **chronic bronchitis**.

N.B. In many cases, signs of emphysema and chronic bronchitis may be present together. Then, the diagnosis is chronic bronchitis with emphysema.

Q: What are your **differential** diagnoses?

A: As follows:

- Chronic persistent bronchial asthma.
- COPD.
- Bilateral extensive bronchiectasis.
- Chronic LVF.

Q: What is **chronic bronchitis**?

A: It is defined clinically as 'the presence of cough, productive of sputum, not attributable to other causes, on most of the days, for three consecutive months, at least for two successive years'.

Q: What are the **causes** of chronic bronchitis?

A: Multiple factors are responsible:

- Smoking.
- Exposure to dust, fume, foggy environment (may be occupational). Dampness, sudden change in temperature—all exaggerate chronic bronchitis.
- Infection (*H. influenzae, S. pneumoniae, Moraxella catarrhalis*: All of these exaggerate chronic bronchitis.)

Q: How does the patient **presents** with chronic bronchitis?

A: It is common in smokers. Usual presentations are:

- Cough with sputum: Cough is more marked in the morning on exposure to cold and during winter. The sputum is mucoid or mucopurulent, usually not associated with haemoptysis.
- Tightness of the chest and breathlessness on exertion.
- At advanced stage, features of pulmonary hypertension and cor pulmonale are present. The patient looks as blue bloater (cyanosed and oedematous).

Q: What **investigations** should be done in chronic bronchitis?

A: As follows:

1. Full blood count.
2. Chest X-ray PA views (no significant abnormality).
3. ECG. (Usually normal. In cor pulmonale, there may be features of RVH.)
4. Lung function tests:
 - FEV_1 (reduced).
 - FVC (reduced).
 - Ratio of FEV_1:FVC is also reduced (indicates obstructive airway disease).
 - Other tests: Residual volume (RV) is increased, total lung capacity (TLC) is increased, gas transfer (either normal or mildly reduced).
5. PEFR (reduced).
6. Blood gas analysis:
 - PO_2 (reduced).
 - PCO_2 (normal or increased).
 - pH (acidosis).
7. CT scan in some cases.

Q: What are the **complications** of chronic bronchitis?

A: As follows:

- Respiratory failure—both type I and type II.
- Emphysema.
- Secondary polycythaemia.
- Secondary infection.
- Pulmonary hypertension.
- Cor pulmonale.

Q: How to **treat** chronic bronchitis?

A: As follows:

1. Smoking must be stopped.
2. Avoid air pollution (dust, fume).
3. Control of infection with appropriate antibiotic.
4. Bronchodilator:
 - Inhaled β-agonist: Salbutamol (200 µg 4–6 hourly), terbutaline.
 - Inhaled antimuscarinic: Ipratropium (40 µg 4 hourly), tiotropium (18 µg daily), oxitropium (200 µg BD).
 - Long-acting β-agonist: Salmeterol, formoterol.
 - Oral theophylline (in some cases).
5. Inhaled corticosteroid beclomethasone (400 µg BD) or budesonide or fluticasone. In severe case, oral prednisolone 30 mg for 2 weeks, followed by maintenance dose.
6. Mucolytic agents like bromhexine or *N*-acetylcysteine (200 mg 8 hourly orally for 8 weeks) may be given.
7. Other measures:
 - Chest physiotherapy.
 - Exercise and weight reduction, if obese.
 - Long-term domiciliary oxygen.
 - Pulmonary rehabilitation.
 - Annual influenza vaccine, 5 yearly pneumococcal vaccine and *Haemophilus influenzae* vaccine may be given.

Q: How to **treat** acute exacerbations?

A: As follows:

- Nebulized bronchodilators like terbutaline, ipratropium bromide.
- IV antibiotic to control infection.
- Oxygen inhalation (24%, 1–3 L/min).
- IV hydrocortisone and oral steroid. (Steroid is only used in acute exacerbations; and, unlike in asthma, it does not influence the course of chronic bronchitis.)

Emphysema

Presentation of a Case

Inspection:

- Chest is barrel shaped.
- Indrawing of the lower intercostal space on inspiration (due to low, flat diaphragm).

Palpation:

- Trachea is central, tracheal tug (descent of trachea during inspiration) is present.
- Cricosternal distance (distance between suprasternal notch and cricoid cartilage): Reduced (normally three fingers or more).
- Apex beat is not felt.
- Chest expansion: Reduced (tell in centimetre).
- Vocal fremitus: Reduced.

Percussion:

- Hyperresonance in both the lung fields.
- Obliteration of the liver and cardiac dullness (liver dullness may be lowered down).

Auscultation:

- Breath sound: Diminished, vesicular with prolonged expiration.
- Vocal resonance: Reduced.

My diagnosis is **emphysema.**

N.B. If plenty of rhonchi are present with above findings, diagnosis is chronic bronchitis with emphysema.

Q: What **investigations** should be done in emphysema?

A: As follows:

1. X-ray chest P/A view (shows features of emphysema):
 - Increased translucency of both lung fields with loss of peripheral vascular markings.
 - Low, flat diaphragm.
 - Tubular heart.
 - Widening of intercostal space and ribs appear horizontal.
 - Bulla may be present (which is pathognomonic).
 - Prominent pulmonary arterial shadow in both hilums (due to pulmonary hypertension).
2. Lung function tests:
 - FEV_1 and FVC are reduced. Ratio of FEV_1:FVC is reduced (obstructive type).
 - Postbronchodilator FEV_1 is <80% predicted, and ratio of FEV_1:FVC is <70% predicted.
 - PEFR: Reduced.
 - Lung volume with increased TLC and RV.
3. Arterial blood gas analysis:
 - Low PCO_2 (due to hyperventilation).
 - Low PO_2.
 - Impaired gas transfer of CO.
4. Other investigations:
 - TC, DC, Hb%, ESR (polycythaemia may be present).
 - CT scan of the chest, especially HRCT: Highly suggestive.
 - To confirm: Biopsy of the lung tissue (not a routine test).
 - In young patient, serum level of α_1-antitrypsin may be done.
 - ECG may show tall P, right ventricular hypertrophy (RVH), right axis deviation (RAD) in patient with cor pulmonale.
 - Echocardiography.

Q: What is the **definitive diagnosis** of emphysema?

A: Histopathological (but not done routinely).

Q: What is **emphysema?**

A: It is the permanent distension of alveoli with destruction of their walls distal to the terminal bronchioles.

Q: What are the **presentations** of emphysema?

A: Breathlessness on exertion and minimum cough with lip pursing.

Q: What are the **types** of emphysema?

A: Four types:

- Centriacinar: Involves the proximal part of acini, limited to respiratory bronchiole with relatively less change in acinus.
- Panacinar: All the alveoli and alveolar ducts in acinus are involved, both central and peripheral portion. It occurs mostly in α_1-antitrypsin deficiency.
- Paraseptal: Along the septa, blood vessels and pleura.
- Scar or irregular emphysema: Scarring and damage affecting the lung parenchyma without involving acinus structure.

Q: What are the **causes** of emphysema?

A: As follows:

- Smoking.
- Cold, dust (centrilobular).
- α_1-antitrypsin deficiency.
- Macleod syndrome (unilateral emphysema).

Q: How **smoking** causes emphysema?

A: Certain mechanisms are responsible:

- Prolonged smoking causes inflammation in airways, release of oxidants and proteinase from inflammatory cells, which are responsible for irreparable damage to supporting connective tissue of alveolar septa.
- There is increased proteinase synthesis and inactivation of antiproteinase due to enzymes responsible for inactivating antiproteinase.
- Imbalance between proteinase and antiproteinase.

Q: Why **lip pursing** is present in emphysema?

A: By this in expiration through partly closed lips, there is increased end-expiratory pressure that keeps airway open, helping to minimize air trapping.

Q: What are the **complications** of emphysema?

A: As follows:

- Pulmonary hypertension.
- Cor pulmonale.
- Respiratory failure type 1.
- Bullae, which may rupture causing pneumothorax.
- Secondary infection.
- Polycythaemia.

Q: What are the **signs of emphysema**?

A: As follows:

- The patient is dyspnoeic with lip pursing.
- Barrel-shaped chest.
- Suprasternal and supraclavicular excavation during inspiration.
- Prominent sternomastoid and scalene muscles.
- Tracheal tug.
- Reduced cricosternal distance (length of trachea above suprasternal notch).
- Indrawing of lower intercostal space during inspiration.
- Horizontal ribs with wide intercostal spaces.
- Wide subcostal angle.
- Obliteration of liver and cardiac dullness.

Q: How to **treat** emphysema?

A: As follows:

1. Smoking must be stopped.
2. For breathlessness:
 - Inhaled salbutamol (200 mg 4–6 hourly) or ipratropium (40 mg 4 hourly) or tiotropium (18 mg daily) or oxitropium (200 mg BD).
 - If no response, inhaled corticosteroid beclomethasone (400 µgm BD).
 - In severe case, oral prednisolone 30 mg for 2 weeks, followed by maintenance dose.
3. Antibiotic, if secondary infection.
4. In chronic cough: Mucolytic therapy (acetylcysteine 200 mg 8 hourly orally for 8 weeks).
5. Domiciliary O_2 may be given.
6. Vaccination, such as annual influenza vaccine, five yearly pneumococcal vaccine and *Haemophilus influenzae* vaccine may be given.
7. Other treatment:
 - α_1-antitrypsin in case of deficiency.
 - Lung transplantation in young patient.
 - Surgical intervention (if large bullae).
 - Weight reduction, if obese.
 - Exercise.

Q: What is **bullae**? What are the **causes**? What is the **treatment**?

A: It is the thin-walled air space produced by rupture of alveolar walls. Bullae may be single or multiple, large or small, and usually associated with emphysema. It is usually situated subpleurally. Rupture may lead to pneumothorax. Large bullae may compress the lung tissue and impair lung function. The causes of bullae are:

- Emphysema.
- Congenital (rare).

Treatment:

- Small bullae: No treatment, treatment of primary cause.
- Large bullae with impaired lung function require surgical ablation of bullae.



Bullae

Q: What is **pink puffer** and **blue bloater**?

A: As follows:

Pink puffer:

- The patient is not cyanosed (pink), but dyspnoeic with lip pursing (puffer). No oedema.
- Usually lean and thin.
- It is found in emphysema, commonly panacinar, of age 50–75 years.
- Usually there is no cor pulmonale.
- Exertional dyspnoea is the main feature, and cough less common.
- Arterial PO_2 and PCO_2 are relatively normal.

Blue bloater:

- The patient is cyanosed (blue) and oedematous (bloater). But not dyspnoeic (or mild dyspnoea).
- It is found in chronic bronchitis, age 40–45 years. Oedema is due to cor pulmonale.
- Cough with sputum is the main feature, dyspnoea is less common.
- Pulmonary hypertension, right ventricular hypertrophy, cor pulmonale and secondary polycythaemia may develop (patient may appear plethoric).
- There is marked arterial hypoxaemia and hypercapnia (low PO_2 and increased PCO_2).

Brief Discussion About Lung Function Test (Spirometry)

Spirometry is a method of assessing the lung function. FEV_1 and FVC are measured. The technique involves a maximum inspiration followed by a forced expiration (as long as possible) into the spirometer. FEV_1 is expressed as a percentage of FVC. It is done to diagnose and differentiate obstructive airway disorders (e.g. COPD and asthma) from restrictive diseases (e.g. ILD). It can also be used to determine the severity of asthma and COPD.

By spirometry, five important measures can be detected:

- **FEV_1 (forced expiratory volume in first second):** The volume of air after forced expiration in the first second, after full inspiration.
- **FVC (forced vital capacity):** The total volume of air expired forcibly in one breath after full inspiration.
- **FEV_1/FVC:** The ratio of FEV_1:FVC is expressed as percentage.
- **PEF (peak expiratory flow):** It is the highest flow one can achieve during forceful expiration. It is used as a short-term monitoring tool at a doctor's chamber, or bedside and emergency room during exacerbation. Long-term monitoring of asthma can be done by seeing diurnal variability of PEF at patient's home by maintaining peak flow chart. This is essential for constructing self-management plan.
- **FEF25–75 (forced expiratory flow in 25–75 percentile):** It is the graphical measurement of average expiratory flow in between 25% and 75% of the expiration during FVC manoeuvre. This measurement denotes airflow condition in smaller airways of <2 mm of diameter, which are devoid of cartilages. It is important in smokers (with COPD and emphysema) and in children who cannot produce satisfactory FEV_1.

PEFR: Measurement of PEFR on a regular basis at home with a portable peak flow meter is useful for patient over 5 years of age with moderate-to-severe persistent asthma. The patient is asked to take a full inspiration as far as possible, and then to blow out forcefully into the peak flow meter. PEFR is best used to monitor the progress of the disease and its treatment.

Regular measurement of PEFR on waking, in afternoon and before bed demonstrates the wide diurnal variations in airflow limitations that characterize bronchial asthma. Daily calculation of diurnal variability of PEF provides a reasonable index of asthma stability and severity. Diurnal variability in peak flow is expressed by the following formula:

$$\text{Diurnal variability} = \frac{(\text{Highest PEF} - \text{Lowest PEF}) \times 100}{\text{Highest PEF}}$$

It should be noted that PEF physiologically falls at late night or early morning. But this fall is normally <20% of personal best result. Fall of PEF > 20% in early morning is known as 'morning dipping of PEF'. It is characteristic of uncontrolled asthma.

Spirometry in obstructive airway disease shows that:

- FEV_1 is reduced (<80% of predicted value).
- FVC is reduced.
- FEV_1:FVC ratio is reduced (<75%).

Spirometry in restrictive airway disease shows that:

- FEV_1 is reduced (<80% of predicted value, but in proportion to FVC).
- FVC is reduced (<80% of predicted value).
- FEV:FVC ratio is normal (>75%).

Q: What are the **restrictive** airway disease and **obstructive** airway disease?

A: As follows:

- Restrictive: ILDs, ankylosing spondylitis and kyphoscoliosis.
- Obstructive: Emphysema, chronic bronchitis and bronchial asthma.

Differences between restrictive and obstructive airway disease

Points	Restrictive	Obstructive
FEV_1 and FVC	Proportionately reduced	FEV_1 is markedly reduced and FVC also reduced
FEV_1:FVC	Normal	Reduced
RV	Reduced or normal	Increased
TLC	Reduced	Increased
RV:TLC	Normal or slightly increased	Markedly increased

N.B. Both TLCO and transfer coefficient of carbon monoxide (K_{CO}) are reduced in restrictive airway disease and obstructive airway disease.

Other Tests

1. **Reversibility test:** Bronchodilator reversibility test can be used to differentiate between asthma and COPD. After bronchodilatation, both >12% and >200 mL increase in FEV_1, over prebronchodilator level indicates positive reversibility test, suggesting diagnosis of bronchial asthma. Negative result indicates COPD (or severe persistent asthma).
2. **Bronchoprovocation test:** In fall of FEV_1, > 20% after inhalation of methacholine or hypertonic saline is used for diagnosis of hyperresponsiveness of airways in susceptible patients with normal spirometry. Susceptible patients are those with: (i) cough-variant asthma, (ii) mild intermittent asthma, and (iii) chronic bronchitis with hyperresponsive airways.
3. **Exercise challenge test:** In fall of FEV_1, or PEFR > 15% from baseline value after vigorous exercise (i.e. running or climbing stairs for 6 min) indicates 'exercise-induced asthma'. Fall starts at 5–10 min after stoppage of exercise and peak at 20–30 min and then resolves automatically. It can be reversed quickly using bronchodilator inhaler.

Bedside Assessment of Lung Function

- If your diagnosis is COPD, forced expiratory time (FET) should be seen by asking the patient to exhale forcefully through open mouth after full inspiration, while you listen by placing your stethoscope over the trachea. Normally, it is <6 s. If >6 s, then it indicates airway obstruction.
- Peak flow meter (as described above).
- Flow volume curve is an alternative to spirometry. Flow volume curve may be measured using a portable electronic device.

Mass Lesion in Lung (Bronchial Carcinoma)

Mass lesion in lung may be isolated bronchial carcinoma without definitive signs. There may be collapse or pleural effusion, or SVC obstruction and radiation mark in chest.

The patient is middle-aged or elderly, emaciated or cachexic with generalized clubbing and nicotine stain in fingers.

Presentation of a Case

(Supposing right-sided lesion)

On inspection:

- Restricted movement of upper part of chest.
- There is radiation mark on the chest (if any).

On palpation:
- Trachea: Central and apex beat in normal area.
- Vocal fremitus: Reduced or absent (rib tenderness may be present).

On percussion:
- Dullness in right upper part of chest (mention up to which space).

On auscultation:
- Breath sound is reduced or absent.
- Vocal resonance is reduced or absent.

My diagnosis is **bronchial carcinoma.**

Q: What **relevants** do you like to see?
A: As follows:

- Hand: Clubbing with nicotine stain, hypertrophic osteoarthropathy, wasting of small muscles of hand (due to involvement of lower trunk of brachial plexus).
- Supraclavicular, axillary lymph nodes (metastasis).
- Eye: Horner syndrome (in Pancoast tumour).
- Evidence of SVC obstruction.



Clubbing



X-ray showing hypertrophic osteoarthropathy at the lower end of ulna

Q: What will you see in **the eyes** of the patient?
A: I will look for partial ptosis, miosis and enophthalmos, which indicates Horner syndrome. It is commonly found in Pancoast tumour. Fundoscopy may show papilloedema, if secondary metastasis in the brain.

Q: What are the **differential diagnoses**?
A: As follows:
- Pleural effusion.
- Pulmonary tuberculosis.
- Other mass lesions (neurofibroma, dermoid cyst, hydatid cyst, etc.).

Q: Why **not** this is pleural effusion?
A: In pleural effusion, trachea and apex beat are shifted to the opposite side.

Q: Why **not** this is collapse?
A: In collapse, trachea and apex beat are shifted to the same side.

Q: Why not **consolidation?**
A: In consolidation, there is bronchial breath sound and increased vocal resonance.

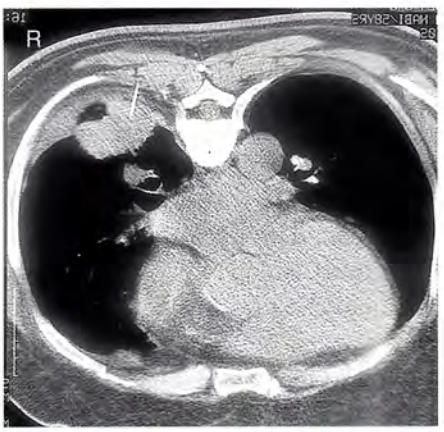
Q: What **investigations** do you suggest in bronchial carcinoma?
A: As follows:

1. X-ray chest PA view (homogeneous irregular opacity with **sun-ray** appearance may be seen. There may be collapse, pleural effusion, hilar lymphadenopathy, widening of mediastinum, raised hemidiaphragm, and rib erosion or destruction).
2. CT scan of chest (MRI is not helpful for primary lesion).
3. Sputum for malignant cells (exfoliative cytology).
4. CT-guided FNAC.
5. FNAC (or biopsy) of lymph nodes (if present).
6. Fibre optic bronchoscopy and biopsy (or bronchial washing and brushing).
7. PET–CT scan is the investigation of choice (highly sensitive and specific for mediastinal staging).
8. To see evidence of metastasis: USG of whole abdomen, X-ray of skull, isotope bone scan, etc. Sometimes, CT scan of chest and abdomen, even MRI may be needed.
9. Others:
 - Complete blood count, ESR.
 - If pleural effusion, then fluid cytology. Pleural biopsy may also be done.

- Liver function test, renal function test (before chemotherapy, if needed).
- Pulmonary function test, specially FEV_1 [diffusing capacity of the lung for carbon monoxide (DLCO) below 60% predicted is associated with a mortality rate of 25% due to pulmonary complications].



Right-sided bronchial carcinoma with phrenic nerve palsy



CT scan showing right-sided bronchial carcinoma

Q: If **sputum** shows malignant cells, would you do **bronchoscopy** and **biopsy**?

A: Yes, to see histological type. This is helpful for therapy and prognosis. If squamous-cell carcinoma, radiotherapy is the treatment. If small-cell carcinoma, chemotherapy is necessary.

Q: Why **bronchoscopy** should be done?

A: Bronchoscopy should be done:

- To see the mass and to take biopsy for tissue diagnosis. This will guide further management.
- If the carcinoma involves first 2 cm of either main bronchus, it indicates that the tumour is inoperable.
- If carina is wide and there is loss of sharp angle of carina, it indicates presence of enlarged mediastinal lymph nodes (may be malignant or reactive). Biopsy can be taken by passing a needle through bronchial wall.
- Vocal cord paralysis on the left indicates left recurrent laryngeal nerve palsy, and indicates an inoperable case.

Q: What are the **types** of bronchial carcinoma?

A: There are two types:

- Non-small-cell carcinoma in 80%.
- Small-cell carcinoma in 20%.

Q: What are the **histological types** of bronchial carcinoma?

A: There are four types:

- Squamous-cell carcinoma in 35%.
- Small-cell carcinoma in 20%.
- Adenocarcinoma in 30%.
- Large-cell carcinoma in 15%.

Features of adenocarcinoma:

- 10% of bronchial carcinoma.
- Arises from mucous cells in the bronchial epithelium.
- Occurs in the periphery of lung.
- Usually develops in or around old scar.
- More in elderly.
- More in female.
- More in nonsmokers.
- More in far East.
- More in asbestosis.
- Invasion to pleura and mediastinal lymph nodes is common.
- Metastasis to brain, bone and adrenal gland is common.

Features of small-cell carcinoma:

- 20–30% of bronchial carcinoma.
- Arises from endocrine cells called Kulchitsky cells. These cells are members of amine precursor uptake decarboxylase (APUD) system, which secretes many polypeptide hormones. Some of these hormones act in an autocrine fashion; they feedback on the cells and cause cell growth.
- Highly malignant, rapidly growing, early metastasis and inoperable at presentation.
- Usually responds to chemotherapy and radiotherapy, less likely to be cured by surgery.
- Overall prognosis is poor. Survival is short, 3 months to 1 year.

Features of bronchoalveolar cell carcinoma:

- Found in 1–2% of bronchial carcinoma.
- Occurs as peripheral solitary nodule or diffuse nodular lesion of multicentric origin.
- It may be associated with profuse mucoid sputum expectoration.



Bronchial carcinoma (emaciated with prominent vein)

Q: What are the **presentations** of bronchial carcinoma?

A: Usually in elderly patients with history of smoking:

1. **Due to lung lesion:**
 - Cough: Dry or sputum production. Changing pattern of regular cough in a smoker is highly suspicious. Bovine cough due to left recurrent laryngeal nerve palsy.
 - Haemoptysis—commonly in central lesion. Sometimes, involvement of large blood vessels causes massive haemoptysis.
 - Breathlessness (due to bronchial obstruction, collapse, or massive pleural effusion or compression of phrenic nerve causing paralysis of the diaphragm).
 - Chest pain (due to involvement of pleura, rib or chest wall, intercostal nerve and brachial plexus).
 - Recurrent pneumonia at the same site or pneumonia with slow resolution is highly suspicious.
 - Apical tumour (called Pancoast tumour) involves cervical sympathetic chain at or above the stellate ganglia, causing Horner syndrome (characterized by ipsilateral partial ptosis, enophthalmos, miosis and anhydrosis of the face). Also, there is pain in shoulder and inner aspect of arm due to the involvement of lower trunk of brachial plexus called Pancoasts syndrome.
2. **Due to local spread in mediastinum:**
 - Hoarseness of voice and a bovine cough (due to involvement of left recurrent laryngeal nerve by left hilar lesion).
 - Dysphagia (oesophageal obstruction, also cardiac tamponade).
 - SVC obstruction (with right-sided mass or mediastinal lymphadenopathy).
 - If pericardium is invaded, there may be pericardial effusion or arrhythmia.
 - Stridor, when lower trachea, carina and main bronchi are narrowed by primary tumour or compression by subcarinal and paratracheal lymph nodes.
3. **Distant metastasis** (in liver, brain, bone, adrenal, contralateral lung and lymph nodes. Metastatic features usually common in adenocarcinoma).
4. **Nonmetastatic–extrapulmonary manifestations** (see below).
5. **General features of malignancy:** Anorexia, weight loss, malaise, fatigue.

Nonmetastatic extra-pulmonary manifestations (paraneoplastic syndrome): Occur in 15–20% cases of bronchial carcinoma due to secretory products by the tumour. These may precede, coincide or follow after the cancer. Treatment of carcinoma improves the features.

1. *Endocrine* (10%, usually in small-cell carcinoma):
 - SIADH (syndrome of inappropriate ADH, usually in small-cell carcinoma).
 - ACTH secretion causing Cushing syndrome (usually in small-cell carcinoma).
 - Carcinoid syndrome (usually in small-cell carcinoma).
 - Hypercalcaemia due to release of parathormone-like substance (usually in squamous-cell carcinoma).
 - Gynaecomastia due to excess oestrogen (in large cell).
 - Rarely, hypoglycaemia and thyrotoxicosis.
2. *Neurological* (in any type):
 - Peripheral neuropathy (usually sensorimotor).
 - Cerebellar degeneration.
 - Cortical degeneration (dementia).
 - Myelopathy: Motor neuron disease-like feature.
 - Retinal blindness (small-cell carcinoma).

3. *Musculoskeletal*:
 - Polymyositis or dermatomyositis (in all types).
 - Myasthenic myopathic syndrome (Eaton–Lambert syndrome).
 - Clubbing and hypertrophic osteoarthropathy (non-small-cell type).
4. *Haematological* (in all types):
 - Migrating thrombophlebitis.
 - **Disseminated intravascular coagulation** (DIC).
 - Thrombotic thrombocytopaenic purpura.
 - Normocytic normochromic anaemia and occasionally haemolytic.
 - Eosinophilia.
5. *Heart* (in adenocarcinoma):
 - Marantic endocarditis (nonbacterial, thrombotic or verrucous endocarditis).
6. *Skin* (in all types):
 - Acanthosis nigricans.
 - Dermatomyositis.
 - Herpes zoster.
7. *Renal*:
 - Nephrotic syndrome due to membranous glomerulonephritis (rare).
8. *Metabolic* (universal at some stage):
 - Loss of weight.
 - Lassitude.
 - Anorexia.

Q: Why **chest pain** in bronchial carcinoma?

A: Due to metastasis in the rib or chest wall invasion.

Q: What is **Pancoast tumour** and **Pancoast syndrome**?

A: As follows:

- **Pancoast tumour** (superior sulcus tumour): It is the tumour that arises from apex of the lung. It may involve the cervical sympathetic chain (at or above the stellate ganglion) causing Horner syndrome.
- **Pancoast syndrome:** This is characterized by pain in the shoulder or inner aspect of arm along the ulnar nerve distribution due to the involvement of lower part of brachial plexus (C8, T1, T2). There may be wasting of small muscles of hand due to C8 and T1 nerve involvement. Local invasion by the tumour may cause pain and tenderness of the first and second ribs with evidence of rib destruction radiologically. Horner syndrome may occur due to involvement of the sympathetic pathway as it passes through T1 root. In Pancoast syndrome, treatment is by combined surgery and radiotherapy.

Q: What are the **causes or risk factors** of bronchial carcinoma?

A: As follows:

- Cigarette smoking is the major risk factor. Even passive smoking causes 1.5 times increase in the risk of bronchial carcinoma.
- Other factors are exposure to asbestos, silica, beryllium, cadmium, chromium, arsenic, iron oxide, radon, radiation, petroleum products and oils, coal tar, products of coal combustion.
- Adenocarcinoma may develop in nonsmokers and in old scar.

Q: How to **treat** bronchial carcinoma?

A: As follows:

1. **Non-small-cell carcinoma:**
 - Surgery should be done, if the tumour is localized to lobe or segment. (It is curative if the stage is T1N0M0.).
 - If surgery is not possible, radiotherapy or chemotherapy or combined therapy should be given.
 - In squamous-cell type, radiotherapy is advised (it is especially indicated in SVC obstruction, repeated haemoptysis and chest pain caused by chest wall invasion or skeletal metastasis).
 - Chemotherapy is less helpful in non-small-cell type.
2. **Small-cell carcinoma:**
 - Even small, metastasis occurs early. Surgery is less helpful. Chemotherapy is usually given. Radiotherapy may be added [continuous hyperfractionated accelerated radiotherapy (CHART) in which total dose is given in smaller; but more frequent fractions offer the best survival].
 - Usual chemotherapy: Intravenous CDV (cyclophosphamide, doxorubicin and vincristine) or CE (cisplatin plus etoposide). Chemotherapy is given every 3 weeks for 3–6 cycles.
3. **Other treatments:** These are usually palliative.
 - Laser therapy with fibreoptic bronchoscopy.
 - Endobronchial therapy: Tracheobronchial stent, cryotherapy, laser, brachytherapy (a radioactive source is placed closed to the tumour).
 - Radiofrequency thermal ablation (RFT).
 - Pleural drainage or pleurodesis (in pleural effusion).
 - Drug: Steroid to improve appetite, morphine or diamorphine for pain (along with laxatives, if constipated). Oral candidiasis should be treated.
 - Short courses of palliative radiotherapy are helpful for bone pain, severe cough or haemoptysis.

RFT is helpful in some malignancy such as bronchial carcinoma and hepatocellular carcinoma. It is done by placing special needle into the tumour under guidance of CT scan. Electric current from radiofrequency current generator is passed through the needle, which results in generation of heat causing destruction of tumour. RFT is helpful, if the tumour size is <4 cm. Also, sometimes used in large tumour.

Complications of RFT:

- Bleeding.
- Pneumothorax.
- Skin burn.
- Secondary infection and lung abscess.

TNM classification of lung cancer (it is for non-small-cell carcinoma)—

- T: Extent of primary tumour.
- N: Involvement of lymph node.
- M: Presence of distant metastasis.

Stages for T:

- Tx: Positive cytology only.
- T1: <3 cm in diameter.
- T2: >3 cm in diameter or extends to hilar region or invades visceral pleura or partial atelectasis or extends into main bronchus, but remains 2 cm or more distal to carina.
- T3: Involvement of chest wall, diaphragm, pericardium, mediastinum, pleura, total atelectasis, main bronchus <2 cm distal to carina.
- T4: Involvement of heart, great vessels, trachea, oesophagus, malignant effusion, vertebral body, carina. Separate tumour nodules.

Stages for N

- N0: No nodal involvement.
- N1: Peribronchial, ipsilateral hilar or intrapulmonary lymph node involvement.
- N2: Ipsilateral, mediastinal or subcarinal.
- N3: Contralateral mediastinal, scalene or supraclavicular.

Stages for M

- M0: No distant metastasis.
- M1: Distant metastasis.

Q: What is the **role of staging?**

A: Staging is done to see the possibility of surgical resection of the carcinoma. TNM staging is done for non-small-cell cancer only. In early stage, surgery may be curative. In advanced stages, surgery may not be possible. Small-cell carcinoma is treated according to whether it is limited or extensive.

Q: What is the **role of surgery** in lung carcinoma?

A: In non-small-cell carcinoma without metastasis, surgery is the treatment of choice. But it has limited role in small-cell carcinoma, as >90% patients have metastasis at the time of presentation.

Q: What are the **contraindications** of surgery?

A: As follows:

- Distant metastasis (M1).
- Invasion of central mediastinal structures including heart, great vessels, trachea and oesophagus (T4).
- Malignant pleural effusion (T4).
- Contralateral mediastinal lymph node involvement (N3).
- $FEV_1 < 0.8$ L.
- Poor general condition, severe or unstable cardiac, or other medical problem.

N.B. Remember the following points:

- In a fit individual, surgery is not absolutely contraindicated in case of direct extension of tumour into the chest wall, diaphragm, mediastinal pleura or pericardium, or to within 2 cm of the main carina.
- Surgery is rarely appropriate in patients over 65 years as the operative mortality rate exceeds the 5-year survival rate.

Q: What are the **indications of radiotherapy?**

A: As follows:

1. As the main treatment in:
 - Localized tumour where surgery is not possible.
 - Along with chemotherapy in small-cell carcinoma.
 - Before and after surgery in selected patients.
2. As a palliative therapy in:
 - Pain (local or metastasis).
 - SVC obstruction.
 - Pancoast tumour.
 - Obstruction of trachea and main bronchi.
 - Recurrent haemoptysis.

Q: What is the role of **chemotherapy**?

A: Small-cell carcinoma is usually treated with chemotherapy. Drugs used are cisplatin, etoposide, cyclophosphamide, vinblastine, vindesine, carboplatin. Newer drugs are docetaxel, paclitaxel, irinotecan, vinorelbine, gemcitabine.

Q: What is the **prognosis**?

A: If it is localized and surgical resection is possible, the prognosis is good. Otherwise:

- Non-small-cell carcinoma: 50% 2-year survival without spread, 10% with spread.
- Small-cell carcinoma: Median survival is 3 months if untreated, 1–1½ year with treatment.

CHAPTER 4

ABDOMEN

"The art of medicine consists of amusing the patient while nature cures the disease"

–Voltaire

Introduction

Usual instructions by the examiner are:

- Examine the abdomen or examine the abdomen and see the relevants.
- Palpate the abdomen. What are your findings?
- Look at the abdomen (in a case of distended abdomen, localized or generalized). What do you think are the causes in this case?

Once asked to examine the abdomen, very likely findings are:

- Splenomegaly.
- Hepatomegaly.
- Hepatosplenomegaly.
- Abdominal mass (in epigastrium, right or left iliac fossa, flanks, central or lower abdomen, renal mass bilateral or unilateral, polycystic kidney and transplanted kidney).
- Ascites or ascites with splenomegaly or hepatomegaly.
- Abdominal aneurysm.
- Normal abdomen.

In majority of the cases, there will be splenomegaly, hepatomegaly, hepatosplenomegaly and, sometimes, abdominal mass or ascites. Keeping **these** in mind, examine carefully and present the case systematically. At the same time, you must be ready to answer the relevant questions, e.g.:

- Suppose the patient has splenomegaly or hepatomegaly or hepatosplenomegaly. Examiner may ask, 'What are the **causes?** What **investigations** do you suggest? '
- Suppose the patient has a mass in epigastrium or iliac fossa. Examiner usually asks, 'What do you think are the **causes?** What **else** do you want to see? What **investigations** do you suggest?'
- If the abdomen is distended, examiner may ask, 'What are the **causes of abdominal distension**? Do you think the patient has **ascites**? How to **confirm** ascites?'
- There may be engorged veins. Examiner asks, 'What are the **causes of engorged vein**? What **else** do you like to see? ' (to see the flow of blood).
- If multiple striae are present, examiner may ask, 'What are the **likely causes?**'

Sometimes the examiner may ask you to examine a normal abdomen to see whether you can examine properly. Be careful; you must not describe findings that are not present. Sometimes a finding may be missed (e.g. small spleen or liver or mass). In such a case, a good examiner may tell or give you a chance, **'see again'**. If this happens, probably you have missed a finding like a just-palpable spleen, liver, mass, etc. In such situations, definitely you have missed some finding and should examine more carefully.

Examination Routine (Abdomen)

Proceed as follows:

- Introduce yourself; ask for permission, 'May I examine your abdomen please?'
- Remain on the right side; ensure that the patient is lying flat in a supine position (remove any extra pillow with permission), hands by the side, abdomen exposed from inframammary region to just above the pubic symphysis (do not expose the genitalia to embarrass the patient).
- Quickly look from head to foot. May be you find some clue for diagnosis. For example, chronic liver disease (CLD), chronic renal failure (CRF)

or other renal diseases [nephrotic syndrome and acute glomerulonephritis (AGN)]. In hereditary haemolytic anaemia, frontal and parietal bossing, mongoloid facies and so on.

Inspection:

- Shape of abdomen may be normal, distended or shrunken (scaphoid). If distended, generalized or localized (epigastrium, right or left hypochondrium, iliac fossa or central part).
- For movement of abdomen ask the patient to take deep breath in and out, inspect from either leg- or head-end to see whether the movement is equal at all sides.
- Visible peristalsis.
- Visible pulsation (in epigastrium).
- Umbilicus (inverted or everted).
- For visible veins, mention the location ... (central part, flank, below or above umbilicus, around umbilicus). If present, **see the flow**.
- If striae, mention the location (colour, size, vertical or horizontal).
- Any scar mark (due to surgery or trauma), fistula (Crohn disease) or stoma (colostomy, ileostomy and ileal conduit).
- Pigmentation (linea nigra from below umbilicus, erythema ab igne).
- Swelling or mass (mention the location ...; also mention whether it is intra-abdominal or extra-abdominal).
- Campbell de Morgan spot may be small, red, nodular lesion (in middle age or elderly).
- Finally, look at the groin to see hernia (ask the patient to cough), pubic hair and genitalia (with permission of the patient).

Palpation:

- Enquire any pain in the abdomen (examine this part in the end) and tell the patient, 'Please tell me, if I hurt you.'
- Ensure that your hand is warm; put the palm gently rather than tip of fingers, keeping the hand flat on abdominal wall with a gentle flexion of metacarpophalangeal (MCP) joints.
- Better if you are in horizontal position by kneeling at the patients side, wrist and forearm in same horizontal plane.
- During palpation, look at face to see whether patient **winces** with pain.

N.B. If ascites, do not forget to palpate by **dipping** technique.

Palpate the abdomen in the following way:

1. First, perform superficial palpation, feel for rigidity or any mass. Hard periumbilical lymph node [called **Sister Mary Joseph nodule** is highly suggestive of metastasis from pelvic or gastrointestinal tract (GIT) primary tumour].
2. Tenderness (rebound tenderness may be seen, press the abdomen slowly and then release suddenly; presence of pain indicates peritonitis).
3. **Liver:** Start from right iliac fossa, ask the patient, 'turn your face to left side, keep your mouth open, take deep breath in and out'. Press and proceed during inspiration and look at the patient's face.

 If liver is **palpable,** see the **following points:**
 - Measure in centimetre (with tape, measure from costal margin in right midclavicular line, and **not finger** measurement). If left lobe is enlarged, measure from xiphoid process.
 - Margin (round or smooth or sharp).
 - Surface (smooth or irregular).
 - Tenderness.
 - Consistency (soft or firm or hard).
 - Upper border of liver dullness (using heavy percussion, but percussion of lower border using light percussion).
 - Auscultation over liver for **bruit** or **rub** (often forgotten).

 N.B. Pulsatile liver may be present. In such a case, put your left hand on the back, right hand over the liver, press gently and see movement of right hand.

4. **Spleen:** Keep your left hand in lowermost part of left side of chest posterolaterally with slight pressure. Starting from the right iliac fossa, ask the patient, 'turn your face to left side, keep your mouth open, take deep breath in and out'. **If it is not felt, turn the patient halfway towards right and palpate again.**

 Once spleen is palpable, see the following points:
 - Measure in centimetre along its long axis from costal margin in anterior axillary line towards right iliac fossa (or from costal margin in left midclavicular line).
 - Feel splenic notch.
 - See, get above the swelling of spleen (insinuate right index finger between spleen and left costal margin).
 - Percuss over spleen and continue up to left lower part of chest (to see the continuation of splenic dullness).
5. Palpate both right and left kidneys (by ballottement).
6. Gall bladder.

7. Any mass (see below).
8. Feel for para-aortic lymph nodes (by tip of fingers).
9. Palpate hernial orifice (ask the patient to cough, see and palpate).
10. Palpate testis (with permission of patient).
11. Finally, PR examination (if the examiner asks). **Never done in the examination.**



Sister Mary Joseph nodule

Percussion:

- Usually a light percussion is done. Note normal tympanic sound.
- See area of liver dullness and splenic dullness.
- If there is suspicion of ascites, see shifting dullness.
- Fluid thrill (if tense ascites).

Auscultation:

- Auscultate; normal bowel sound.
- Over liver (hepatic bruit or rub).
- Renal bruit (2 cm above the umbilicus and lateral to midline).
- Bruit of aortic aneurysm (if any).
- Splenic rub (rarely found).
- Venous hum (heard between xiphisternum and umbilicus). It is a continuous, low-pitch soft murmur. Presence of venous hum indicates portal hypertension (rare finding). It is due to large volume of blood flowing in umbilical or paraumbilical vein in falciparum ligament due to portosystemic shunt.

N.B. When venous hum is present with prominent veins in anterior abdominal wall, it is called **Cruveilhier–Baumgarten syndrome**.

After finishing, ask permission, 'May I see the relevants please?" or the examiner may ask, "What relevants do you like to see?'

Relevant findings to be seen according to your findings in abdomen and suspicion of causes:

- If the patient has ascites and splenomegaly that may be due to CLD, your answer will be, 'I want to see the stigmata of CLD' (see page 202).
- If the patient has splenomegaly or hepatosplenomegaly, which may be due to lymphoma, leukaemia or CLD, your answer will be, 'I want to see lymph nodes in other parts of the body, bony tenderness, anaemia or stigmata of CLD'.
- In young age, if the patient has splenomegaly or hepatosplenomegaly, which may be due to hereditary haemolytic anaemia, your answer will be, 'I want to see anaemia, jaundice, frontal and parietal bossing in head, prominent malar bones or mongoloid facies, also family history'. If chronic liver disease (CLD) is suspected, examiner may ask, **'What specific signs** do you like to see in a child or young age?' Your answer is 'KF ring in eye (Wilson disease) and emphysema in chest (α_1-antitrypsin deficiency)'.
- If mass in epigastrium, which may be due to carcinoma of stomach, your answer will be, 'I want to see the left supraclavicular lymph node' (Virchow gland).
- If you find a renal mass and the patient looks anaemic, look for arteriovenous (AV) fistula in the wrist or below the clavicle (haemodialysis); also look for blood pressure (BP), puffy face and oedema.

If you get any mass, see the following points:

First of all, see whether it is intra-abdominal or extra-abdominal. Ask the patient to raise his head and press over the forehead. Now, see and palpate the mass again. If it disappears or is less prominent, it is intra-abdominal. If it is more prominent, then it is likely to be extra-abdominal. Next, see the following points:

- Site.
- Size.
- Shape (round, regular or irregular).
- Surface (smooth or irregular).
- Consistency (soft or firm or hard).
- Tenderness.
- Mobility (mobile or fixed).

N.B. A fixed mass that does not move with respiration is highly suggestive of a retroperitoneal (such as retroperitoneal sarcoma) or colonic mass.

Remember, examiner may give clue during instruction and will expect specific answers. For example:

- This patient is referred to you from cardiology unit. Palpate the abdomen. (In such a case, there may be splenomegaly, which is due to infective endocarditis. Or enlarged and tender liver, which

may be due to congestive cardiac failure (CCF) or chronic constrictive pericarditis. Or ascites due to chronic constrictive pericarditis, even CCF).
- Look at the patient and now palpate the abdomen. The patient may have plethoric face. Splenomegaly indicates polycythaemia rubra vera or bilateral renal mass due to polycystic kidney disease.
- Look at the patient (may have rheumatoid hand) and palpate the abdomen (splenomegaly indicates Felty syndrome).
- This young lady has thrombocytopaenia. Now palpate the abdomen [splenomegaly is suggestive of systemic lupus erythematosus (SLE)].
- This patient has extreme itching. Examine the abdomen (splenomegaly is due to polycythaemia rubra vera).
- This lady of 21 years is referred to from neurology having CVD and right-sided hemiplegia. Examine the abdomen (splenomegaly is suggestive of SLE with antiphospholipid syndrome).

Some Important Findings on Inspection

If there are **obvious findings on inspection** examiner may ask, 'What do you see? ', 'What is this? ' and 'What are the causes?' Examples:

Distended abdomen: The causes of generalized distension (five Fs):

- Fat (obesity).
- Fluid (ascites).
- Foetus (in female of child-bearing age).
- Flatus (gastrointestinal).
- Faeces (constipation).

(Others: Intra-abdominal growth, big ovarian cyst, urinary retention).

Causes of **localized** distension:

1. Epigastrium:
 - Left lobe of liver (hepatoma, secondaries, liver abscess and hydatid cyst).
 - Pancreas (pancreatic pseudocyst and carcinoma of head of pancreas).
 - Stomach (carcinoma of stomach and lymphoma).
 - Others include epigastric hernia, aneurysm of aorta (pulsating mass) and growth in transverse colon.
2. Right hypochondrium:
 - Hepatic mass (hepatoma, secondaries, liver abscess and hydatid cyst).
 - Gall bladder (carcinoma, mucocoele, empyema and carcinoma of head of pancreas).
 - Mass in hepatic flexure or right side of transverse colon (carcinoma colon).
3. Left hypochondrium:
 - Splenomegaly (due to any cause).
 - Renal mass and suprarenal mass.
 - Mass in splenic flexure or left side of transverse colon (carcinoma colon).
 - Hydatid cyst.
 - Carcinoma of pancreas (from tail).
4. Hypogastric swelling (below umbilicus):
 - Bladder (urinary retention).
 - In female (ovarian cyst and pregnancy).
 - Intra-abdominal malignancy.
 - Lymphoma.
 - Tabes mesentericus or mesenteric cyst.
 - Hydatid cyst.



Upper abdominal swelling



Lower abdominal distension (urinary retention)

Causes of **scaphoid abdomen** (shrunken):

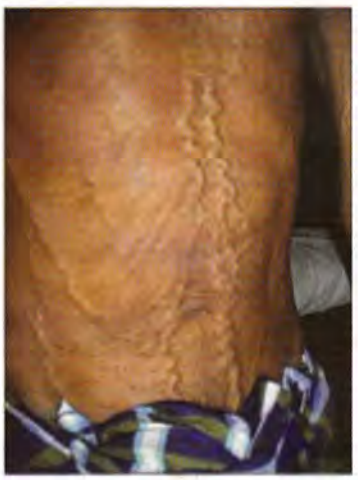
- Starvation.
- Carcinoma (commonly, oesophagus and stomach).



Scaphoid abdomen

Causes of **engorged veins:**

1. Superior vena caval (SVC) obstruction (flow is downwards).
2. Inferior vena caval (IVC) obstruction (flow is upwards).
3. Portal obstruction (like normal flow) as follows:
 - Veins above umbilicus (flow is upwards).
 - Veins below umbilicus (flow is downwards).
4. In extreme cachexia, engorged veins are present due to loss of subcutaneous fat.
5. Normally present in lean and thin person.



Engorged veins

Q: If **engorged vein**, examiner may ask, 'What else would you like to see and why?'

A: I want to see the flow of blood to find out causes (see above).

Q: What is the **normal blood flow** of veins?

A: As follows:

- Veins above umbilicus (flow is upwards).
- Veins below umbilicus (flow is downwards).

Q: How to **differentiate** between SVC obstruction, IVC obstruction and portal obstruction?

A: For differentiating features see the table given below.

	SVC obstruction	IVC obstruction	Portal obstruction
Veins	Usually in the upper abdomen and chest wall	Mostly in the flanks and rarely in the lower abdomen	In the upper and in the lower abdomen, also around the umbilicus (caput medusae)
Flow	Downwards	Upwards	Away from the umbilicus (flow of veins upwards above the umbilicus and downwards below it)

N.B. There will be other signs of SVC, IVC or portal vein obstruction.

Q: What are the **signs of SVC obstruction**?

A: As follows:

- Face is plethoric or reddish, oedematous or puffy, suffused.
- Eyes with conjunctival suffusion, chemosis and periorbital oedema.
- Neck veins are engorged and nonpulsatile.

Q: What are the **signs of IVC obstruction**?

A: As follows:

- Engorged vein in lower limbs.
- Lower limbs: Swollen and oedematous.
- Also buttock and groin: Swollen and oedematous.

N.B. In IVC obstruction, engorged veins are due to dilated anastomotic channel between superficial epigastric and circumflex iliac veins below and lateral thoracic veins above, conveying blood from long saphenous vein to axillary vein.

Q: What are the **signs of portal obstruction**?

A: As follows:

- Splenomegaly (the single most definitive sign).
- Ascites.
- Oesophageal varices by endoscopy and also haemorrhoid by proctoscopy.

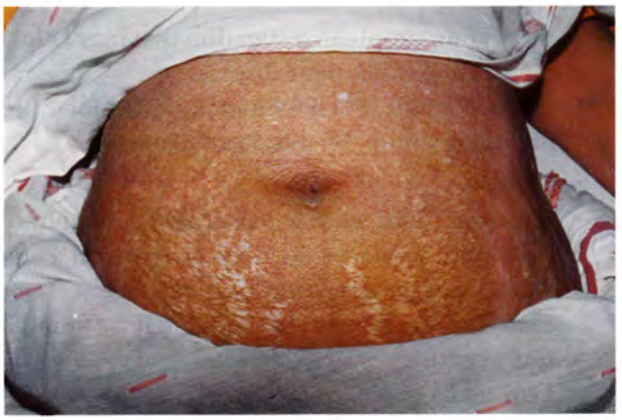
Q: What is **caput medusae**?

A: Caput medusae refer to dilated veins radiating from the umbilicus, found in portal obstruction. It is named after its resemblance to the Greek goddess *Medusae*, whose head was adorned with snakes that radiated from her head (*Caput* means head). It is a rare finding.

Q: What are striae? What are the causes?

A: These are wrinkled, linear, white or pink-coloured marks over the skin. Striae are due to stretching of skin causing rupture of elastic fibres. Causes of striae are:

- Striae gravidarum (white or pink, narrow lines, in abdominal walls due to pregnancy, and usually below the umbilicus).
- Obesity (whitish narrow lines, usually longitudinal, < 2 mm).
- Cushing syndrome. (Wide lines, pink or purple or red, mostly horizontal or oblique. Pink or red colour is due to increased vascularity.)
- Ascites.



Striae gravidarum

Causes of visible epigastric pulsation:

- Normally, in thin body build.
- Right ventricular hypertrophy.
- Aneurysm of the aorta.
- Pulsatile liver.
- Mass overlying the abdominal aorta (e.g. carcinoma stomach).

Causes of eversion of umbilicus:

- Ascites (slit is transverse).
- Ovarian cyst (slit is vertical).
- Umbilical hernia.

Causes of multiple fistula in abdomen:

- Crohn disease.
- Tuberculosis (TB).
- Actinomycosis.
- Trauma.

Q: What is Grey Turner sign?

A: It is the skin discolouration in the flanks of abdominal wall due to extraperitoneal bleeding (haemoperitoneum due to any cause).



Grey Turner sign

Q: What is Cullen sign?

A: It is the skin discolouration around the umbilicus, usually a faint bluish hue. It is due to haemoperitoneum.



Cullen sign

Causes of haemoperitoneum:

- Rupture of spleen.
- Rupture of ectopic pregnancy.
- Acute haemorrhagic pancreatitis.
- Any cause of bleeding (blood dyscrasia and excess anticoagulant).

Multiple small, firm skin nodules in the anterior abdominal wall may be due to:

- Neurofibroma.
- Disseminated malignancy (secondaries).
- Sarcoidosis.
- Lipoma.

A hard nodule around the umbilicus called **Sister Mary Joseph nodule** indicates metastasis (from pelvic or GIT tumour).

Q: What is Riedel lobe?

A: It is a tongue-like projection from inferior surface of right lobe of liver, felt in right hypochondrium. It is a normal finding, common in women, rarely may be very large up to the right iliac fossa. It may be confused with enlarged gall bladder or enlarged right kidney.

Hepatosplenomegaly

Presentation of a Case

- The abdomen may be (or is distended) generalized or in right or left hypochondrium.

The liver is (*mention your findings*):

- Enlarged, ... cm from right costal margin in right midclavicular line.
- Margin is sharp or round.
- Surface is smooth, irregular and nodular (single or multiple).
- Consistency is firm (or soft or hard).
- Tender (or nontender).
- Upper border of the liver dullness is in right ... intercostal space, in right midclavicular line.
- There is no (or yes) hepatic bruit (or rub).

The spleen is ... (*mention your findings*):

- Enlarged; ... cm from left costal margin, in left anterior axillary line (towards right iliac fossa).
- Soft or hard or firm in consistency.

My diagnosis is **hepatosplenomegaly.**

Q: What are the **causes** of hepatosplenomegaly?

A: Mention the causes of that patient according to the age:

If the patient is **middle-aged or elderly**, the causes are:

- Kala-azar.
- Malaria.
- Chronic myeloid leukaemia (CML).
- Myelofibrosis.
- Lymphoma.
- CLD with portal hypertension.

If the patient is **young or of early age**, the causes are:

- Kala-azar.
- Malaria.
- Hereditary haemolytic anaemia (ß-thalassaemia major, HbE disease and hereditary spherocytosis).
- Lymphoma.
- CLD with portal hypertension.

Q: What **history** do you like to take?

A: History of fever (malaria, kala-azar, lymphoma and CML), previous history of liver disease and jaundice. In child, there will be a history of growth retardation, anaemia, jaundice and family history of hereditary haemolytic anaemia.

Q: What **else** or **relevants** do you want to see?

A: As follows:

- Lymph nodes (in lymphoma, CLL and viral infection).
- Signs of CLD (page 202).
- Pigmentation (in kala-azar, also CLD and haemochromatosis).
- Bony tenderness (in leukaemia and lymphoma).
- In young or child, anaemia, jaundice, frontal and parietal bossing, mongoloid facies (hereditary haemolytic anaemia).

Causes of CLD with hepatomegaly

- Haemochromatosis.
- Primary biliary cirrhosis.
- Alcoholic liver disease.

Q: Mention **one simple investigation** that may help to diagnose or exclude some diseases.

A: Full blood count (FBC) with peripheral blood film (PBF) examination. By this, I can diagnose:

- Malaria.
- Kala-azar [FBC shows leucopaenia, lymphocytosis and monocytosis. Repeated blood count shows progressive leucopaenia. Rarely Leishman–Donovan body (LD body) may be found in buffy coat].
- Leukaemia.
- Myelofibrosis (pancytopaenia, leucoerythroblastic blood picture, tear- or pear-drop poikilocyte).
- Hereditary haemolytic anaemia (microcytic hypochromic blood picture).
- Multiple myeloma (high ESR and rouleaux formation).

Q: What **investigations** do you suggest in hepatosplenomegaly?

A: As follows:

1. Hb%, TC, DC, ESR, platelet, PBF and malarial parasite.
2. Chest X-ray (in lymphoma and leukaemia, shows bilateral hilar lymphadenopathy).
3. Ultrasonogram (USG) of whole abdomen (lymphadenopathy or other mass).
4. Bone marrow (LD bodies, leukaemia and myelofibrosis).
5. If lymph node is palpable, fine-needle aspiration cytology (FNAC) or biopsy.
6. Other investigations according to suspicion of causes:
 - For kala-azar (see page 183).
 - Investigations for CLD (see page 203).
 - In hereditary haemolytic anaemia (Hb electrophoresis and X-ray of skull).

Pattern Hepatomegaly
↳ + Splenomegaly
↳ + Splenomegaly + Ascites

Causes of hepatosplenomegaly:

1. Infection: Kala-azar, malaria, schistosomiasis (in Middle East and Africa), enteric fever, infectious mononucleosis and cytomegalovirus (CMV) infection.
2. Myeloproliferative diseases:
 - CML.
 - Polycythaemia rubra vera.
 - Myelofibrosis.
 - Essential thrombocythaemia.
3. Lymphoproliferative diseases:
 - Chronic lymphatic leukaemia (CLL).
 - Multiple myeloma.
 - Waldenström macroglobulinaemia.
 - Lymphoma.
4. Cirrhosis of liver with portal hypertension.
5. Others:
 - Collagen diseases (SLE, Sjögren syndrome, Felty syndrome).
 - Sarcoidosis.
 - Amyloidosis.
 - Thyrotoxicosis (in Graves disease, rare).
 - Acromegaly.
 - Storage disease (Gaucher disease and glycogen-storage disease).
 - Polycystic disease.

Q: What are the causes of **lymphadenopathy with hepatosplenomegaly?**

A: As follows:

- Lymphoma.
- Chronic lymphatic leukaemia (may be found in CML with blastic crisis).
- Acute lymphatic leukaemia (ALL).
- SLE.
- Disseminated TB.
- Others include infectious mononucleosis, cytomegalovirus (CMV) infection, HIV, kala-azar (in Chinese, also African kala-azar), sarcoidosis, brucellosis and toxoplasmosis.

Q: What are the causes of **fever with hepatosplenomegaly?**

A: As follows:

- Malaria.
- Kala-azar.
- Enteric fever.
- Viral infection (infectious mononucleosis and CMV infection).
- Lymphoma.
- Leukaemia (CGL, CLL, ALL, AML).
- Collagen disease (SLE).
- Disseminated TB.
- Brucellosis.
- Toxoplasmosis.
- Sarcoidosis.

Hepatosplenomegaly (Malaria)

Presentation of a Case

Present as described previously.

Q: What **investigations** are done to diagnose malaria?

A: As follows:

- Blood film (both thick and thin).
- Rapid antigen detection.

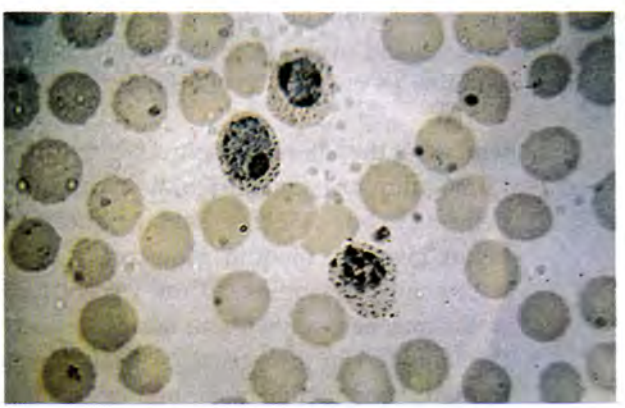
Q: Why **thick** and **thin** films are done?

A: As follows:

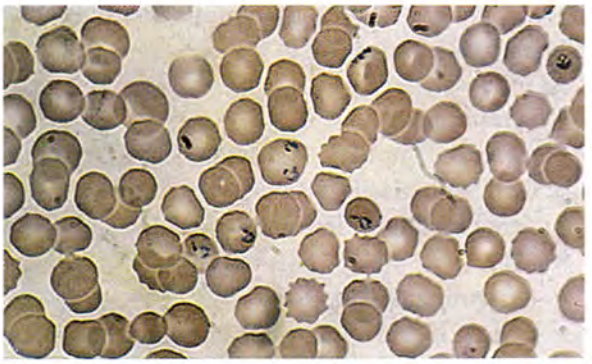
- In thick film, erythrocytes are lysed, releasing all blood stages of parasite. It is helpful to detect the parasite even with low level of parasitaemia.
- Thin film is necessary to detect the species and also to quantify the parasite load in *Plasmodium falciparum*.

N.B. Remember the following points:

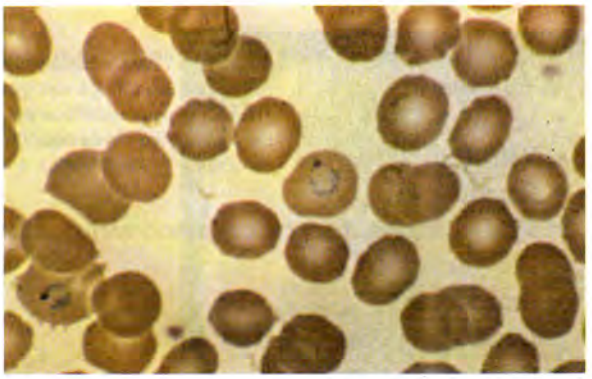
- In falciparum malaria, only ring form is found.
- Other species (*Plasmodium vivax*, *Plasmodium malariae* and *Plasmodium ovale*): All stages of erythrocytic cycle such as ring, trophozoite, schizont and gametocyte are found.
- Gametocytes are found after about 2 weeks.
- Malarial parasites may be found both during febrile, also in afebrile period. But falciparum is difficult to find in afebrile period.
- Usual staining by Leishman or Giemsa.



Plasmodium vivax



Plasmodium falciparum



Plasmodium falciparum **(ring form)**

Q: What are the species having **exoerythrocytic cycle** (hepatic)? How to **treat?**

A: *P. vivax* and *P. ovale* persist in liver cell as dormant form called hypnozoite. This may develop into merozoite months or years later, causing relapse of malaria. For this, after treatment of malaria, primaquine 15 mg daily for 14 days is given to eradicate exoerythrocytic cycle.

P. falciparum and *P. malariae* have no exoerythrocytic cycle, but recrudescence of fever may occur from multiplication of parasite in red cells, not eliminated by treatment and immune process.

Q: What is **radical cure?**

A: It means eradication of hypnozoite of malarial parasite (vivax and ovale) from the liver. It is done by primaquine 15 mg daily for 14 days.

N.B. Remember the following points:

- Primaquine can cause haemolysis in G6PD deficiency. So, G6PD should be measured before giving primaquin. However, if G6PD is present, primaquine 30 mg weekly for 8 weeks may be given without harmful effect.
- Primaquine can also cause cyanosis due to formation of methaemoglobin in red cells (not dangerous).

Q: Why **anaemia** occurs in malaria?

A: Anaemia is due to:

- Haemolysis of infected and uninfected red cells.
- Dyserythropoiesis.
- Splenomegaly (causing sequestration and haemodilution).
- Reduction of folate store.

Q: Which **red cells** are involved by different species of malaria?

A: As follows:

- *Falciparum* involves red cells of all ages. Hence, haemolysis is severe.
- *Vivax* and *ovale* involve mainly reticulocyte. Hence, haemolysis is less severe.
- *Malariae* involves normoblast; it can cause glomerulonephritis and nephrotic syndrome in children.

Q: What is **malignant** malaria and **benign** malaria?

A: As follows:

- **Malignant malaria:** It is due to *P. falciparum* associated with widespread organ damage due to capillary blockage. It is more serious.
- **Benign malaria:** It is mainly due to *P. vivax*, less frequently by *P. ovale* and malariae. Less serious.

Q: What are the features of **severe *P. falciparum* infection?**

A: It may involve any systems in the body. There may be serious complications and death. A high parasitaemia (>1% or RBC infected) is an indicator of severe disease. The features are:

1. CNS: Prostration, cerebral malaria (features are confusion, convulsion, diminished consciousness, coma without localizing sign).
2. Renal: Haemoglobinuria (blackwater fever), oliguria, acute renal failure, acute tubular necrosis.
3. Blood: Severe anaemia, DIC, bleeding.
4. Respiratory: Tachypnoea, acute respiratory distress syndrome, acute pulmonary oedema.
5. Metabolic: Hypoglycaemia (particularly in children), metabolic acidosis.
6. Gastrointestinal/liver: Diarrhoea, jaundice, splenic rupture.
7. Other: Hyperpyrexia, shock.

Q: Which disease or haemoglobinopathy **protects** against malaria?

A: As follows:

- *Falciparum* does not grow well in RBC containing haemoglobin F, C or S. Sickle-cell disease protects against falciparum malaria.
- *Vivax* cannot enter RBC that lacks Duffy blood group (West African and American blacks are protected).

Q: How to **treat** malaria?

A: As follows:

1. For *P. vivax*, *P. ovale* and *P. malariae* (nonfalciparum):
 - Chloroquine: First day 600 mg (4 tablets), then 300 mg (2 tablets) after 6 h. From next day, 150 mg (1 tablet) twice daily for 2 days.
 - For radical cure: Primaquine 15 mg daily for 14 days (after chloroquine).
2. Treatment of falciparum malaria: Many cases are resistant to chloroquine.
 a. Mild or uncomplicated case:
 - Coartemether (artemether plus lumefantrine): 4 tablets stat, 4 tablets after 8 h, and then 4 tablets 12 hourly for 2 days (total 24 tablets).
 - Or, quinine 600 mg (10 mg/kg) 8 hourly for 7 days orally. Dose can be given 12 hourly, if quinine toxicity develops.
 - Some quinine resistance is found. So after quinine, single dose of sulfadoxine 1.5 g plus pyrimethamine 75 mg (Fansidar 3 tablets), or doxycycline 200 mg daily for 7 days or clindamycin 450 mg 8 hourly for 7 days, or Malarone (proguanil plus atovaquone) 4 tablets once daily for 3 days may be given.
 - Artesunate 200 mg daily for 3 days, and mefloquine 1 g on day 2 and 500 mg on day 3 may be used.
 - A new drug called Lapdap (chlorproguanil and dapsone) is in trial.
 b. Complicated or severe falciparum infection or cerebral malaria:
 - Injection artemether 2.4 mg/kg IV at 0, 12 and 24 h and then once daily for 7 days is the treatment of choice. Intravenous (IV) treatment should be replaced by oral therapy (2 mg/kg once daily) when the patient is able to swallow. Total cumulative dose is 17–18 mg/kg (It is a synthetic antimalarial drug, derived from artemisinin, and should be avoided during pregnancy, unless strongly indicated).
 - Artemether may be given in the following dose: 80 mg intramuscular (IM) twice daily for 1 day, followed by 80 mg daily for 4 days or 80 mg IM twice daily for 3 days.
 - Alternatively, quinine IV initially 20 mg/kg (maximum 1.4 g), with 500 cc 5% dextrose in aqua over 4 h, then 10 mg/kg 8 hourly (maximum 700 mg per dose) for 7 days, until patient can take orally. The loading dose should not be given if the patient has received quinine, quinidine or mefloquine during the previous 24 h.
 - Other treatment:
 - Blood transfusion may be needed for severe anaemia.
 - Monitoring and management of water and electrolyte balance, renal failure, hepatic failure, if present. Quinine may cause hypoglycaemia. So monitoring of blood glucose is essential.
 - Exchange transfusion may be helpful with persisting high parasitaemia (>10% circulating erythrocyte).
 - If coma persists, lumbar puncture and CSF study to exclude other diseases such as meningitis or encephalitis.

Q: How to **prevent** malaria in travellers (chemoprophylaxis)?

A: As follows:

1. High chloroquine resistance:
 - Mefloquine 250 mg weekly; started 2–3 weeks before travel and continued until 4 weeks after.
 - Or, doxycycline 100 mg daily; started 1 week before and continued until 4 weeks after travel.
 - Or, malarone (atovaquone-proguanil) 1 tablet daily, from 1–2 days before travel until 1 week after return.
2. No chloroquine resistance:
 - Chloroquine 300 mg base weekly; started 1 week before and continued 4 weeks after travel.
3. Limited chloroquine resistance:
 - Chloroquine 300 mg base weekly and proguanil 100–200 mg daily; both started 1 week before and continued 4 weeks after travel.
 - Or, doxycycline 100 mg daily; started 1 week before and continued until 4 weeks after travel.
 - Or, malarone (atovaquone–proguanil) 1 tablet daily, from 1–2 days before travel until 1 week after return.
 - Or, mefloquine 250 mg weekly; started 2–3 weeks before travel and continued until 4 weeks after.

Q: What are the **complications** of malaria in pregnancy and how to **treat**?

A: As follows:

- Fetal complications: Still birth, low birth weight, foetal distress. High foetal death in falciparum

malaria, especially in the last trimester. Congenital malaria may occur in 5% cases.

- Maternal complications: Maternal death, abortion, premature labour, anaemia, hypoglycaemia and acute pulmonary oedema.

Treatment during pregnancy:

- Chloroquine should be given as a usual dose.
- In *P. vivax* and *P. ovale* infection, no primaquine until delivery. Chloroquine 600 mg weekly should be given and continued until delivery.
- If no response to chloroquine, quinine 600 mg 8 hourly for 1 week.
- In falciparum malaria, quinine 600 mg 8 hourly for 1 week.

Q: What is **pernicious malaria?** Mention the **causes, clinical features** and **treatment?**

A: It is a severe form of falciparum malaria in which there is widespread capillary blockage by the parasitized RBC causing multiple organ damage. If not properly treated, the patient may die within 1–3 days. It occurs when > 5% of RBC are parasitized.

Pathogenesis: Parasitized RBC develop knob-like projections on the surface, becomes sticky and adhere to the endothelium of capillaries of different organs. As a result, there is blockage with severe anoxia and organ damage involving brain, kidneys, heart and GIT. Increased capillary permeability, secondary vasoconstriction and rupture of schizont cause toxin liberation, leading to further organ damage.

Infected RBC also adheres to uninfected RBC to form rosette, causing further blockage. Blood film shows heavy parasites (both schizont and ring form).

Clinical types of pernicious malaria:

- Cerebral type characterized by high fever, coma without focal neurological signs, convulsion, extensor plantar response. CSF study is normal.
- Algid type may be gastric, choleric and dysenteric.
- Septicaemic type is characterized by high fever, pneumonia, cardiac failure, renal failure and jaundice.

Treatment: Similar to complicated falciparum (see above).

Q: What is **blackwater fever?** What is the **mechanism, clinical features** and **treatment** of blackwater fever?

A: It is a severe manifestation of falciparum malaria, occurs in previously infected person, characterized by sudden intravascular haemolysis, fever and haemoglobinuria. It is invariably associated with falciparum malaria, in those who had taken antimalarial drugs irregularly; or in nonimmune person, who had taken irregular antimalarial prophylaxis. It is common in G6PD deficiency.

Mechanism: Actual mechanism is unknown. Probably due to antibody-like haemolysin that is formed due to autoimmune reaction against RBC that have been altered by drug, parasite or both. With some precipitating factors such as cold, trauma and fatigue, there is increased formation and release of haemolysin, causing haemolysis.

Clinical features: High fever with chill and rigour, vomiting, diarrhoea, dark-to-black urine (haemoglobinuria), collapse and renal failure.

Diagnosis: Mostly clinical and by history, malarial parasite is not found in blood during attack.

Treatment:

- Similar to complicated malaria.
- Blood transfusion.
- Prednisolone may be helpful.
- Treatment of renal failure.

Hepatosplenomegaly (Kala-Azar)

Presentation of a Case

Present as described previously.

Differential diagnosis: As in hepatosplenomegaly (see page 178).

Q: What are the **presentations** of kala-azar?

A: Incubation period is 1–2 months (may be months to years, even 10 years).

1. Fever: Usually intermittent, either double or triple rise daily. Sometimes, fever may be irregular, low-grade continuous, occasionally undulant fever (pyrexia followed by apyrexial period). There may be associated chill and rigor.
 - Usually no anorexia, no malaise, no coated tongue.
 - Bleeding (due to thrombocytopaenia).

 Physical findings are:
 - Emaciation.
 - Anaemia (always present, may be severe).
 - Splenomegaly, which may be huge (firm-to-hard).
 - Hepatomegaly.

- Lymphadenopathy: Common in African and Chinese kala-azar, rare in Indian kala-azar.
- Skin: Pigmented, dry thin, scaly. Sometimes there may be diffuse, warty, nonulcerative skin lesion containing parasite.

Q: What is the **appetite** in Kala-azar?
A: Usually good.

Organism: *Leishmania donovani* **complex**

- *L. donovani* (India and South East Asia)
- *Leishmania infantum* (Middle East, Mediterranean area)
- *Leishmania chagasi* (South, Central America)

Source/reservoir: Human (Indian kala-azar).

Mode of transmission:

- Bite by infected female sandfly (common).
- Congenital: Transplacental.
- Blood transfusion.

N.B. Remember the following points:

- Human is the only reservoir in Indian subcontinent.
- Other reservoirs include dog, jackal, fox and wild rodents in other country.
- Leishmania has two forms: Amastigote and promastigote.
- Amastigote form (oval) is found in human; LD body is found in monocyte–macrophage system.
- Promastigote form (flagellate) is found in sandfly, also in culture media.

Q: What **investigations** are done to diagnose kala-azar?
A: As follows:

1. Complete blood count (CBC): Leucopaenia, high lymphocyte and monocyte, neutropaenia, absence of eosinophil, thrombocytopaenia and high ESR. If CBC is repeated after some days, there is **progressive leucopaenia**.
2. Immunological tests based on antibody:
 - Direct agglutination test (DAT): It is called DAT because promastigote is used as an antigen. May be positive after 2 weeks (usually within month). It remains positive years after cure (so it does not indicate active infection). Disadvantage of DAT: Cannot differentiate past, subclinical and active infection. False-positive DAT may occur in leprosy, African trypanosomiasis, TB and hepatitis B.
 - Immunochromatographical test (ICT): Also called rK39 dipstick rapid test.
 - Indirect haemagglutination assay (IHA)
 - Indirect fluorescent antibody test (IFAT)
 - ELISA.
 - Complement fixation test (CFT): It is non-specific, positive after 3 weeks. False positive occurs in TB, leprosy, cirrhosis of liver and multiple myeloma. This test is performed by using Kedrowski bacillus.
 - Aldehyde test: Still helpful where there is no facility. This test is nonspecific and positive when there is associated hypergammaglobulinaemia. It may be false positive in TB, leprosy, cirrhosis of liver, multiple myeloma, SLE, leukaemia and thalassaemia. This test is positive in kala-azar in 2–3 months (negative after 6 months).
3. Detection of antigen: Done by latex agglutination test (Katex) for detecting leishmanial antigen in urine. This test is very simple, more specific than antibody-based test, highly sensitive (96%) and also specific (100%). This test indicates active disease. The antigen is detected in urine within a week and disappears from urine within 3 weeks following successful treatment. Hence, this test is helpful for early diagnosis and also to see the response to therapy.
4. Definitive diagnosis by isolation of Leishman–Donovan (LD) body from bone marrow and spleen puncture; also done from liver, lymph node and skin lesion. Smears are stained by Leishman, Giemsa or Wright stain. Culture is done in NNN media (Nicolle–Nove–McNeal). LD body is positive as follows:
 - Spleen: 90–95% (splenic puncture is avoided in case of soft spleen, prolonged prothrombin time (PT) and platelet count is <40,000/mm^3).
 - Bone marrow and liver: 85%.
 - Lymph node: 65%.
 - LD body is rarely found in peripheral blood in buffy coat preparation. It may also be found in thick film (present in monocyte).
5. PCR (from lymph node or bone marrow aspiration); positive up to 100% case.
6. Blood for total protein and A:G ratio (high total protein, low albumin and high globulin).

N.B. Culture is done for identification of species; and if the number of organisms is less, it may grow in culture media. Organism may grow after 1 week, may take 4 weeks.



LD body

Q: What are the mechanisms of **anaemia** in kala-azar?

A: Due to:

- Hypersplenism (sequestration and splenic pooling, destruction of RBC in spleen).
- Short lifespan of RBCs.
- Haemolysis.
- Ineffective erythropoiesis, infiltration of marrow by parasite.
- Bleeding, haemodilution.

Q: Why **bleeding** occurs in kala-azar?

A: As follows:

- Bleeding may occur before treatment due to thrombocytopaenia.
- Bleeding may occur during treatment with sodium stibogluconate.

Q: Why **bleeding** occurs during treatment with sodium stibogluconate?

A: Actual mechanism is unknown. It may be due to:

- Abnormality in preparation of drug.
- Decomposed or expired date of drug.
- Functional abnormality of platelet by the drug (pentavalent antimony is transformed to trivalent, which may cause thrombasthaenia).
- Bleeding due to other causes (CLD and blood dyscrasias).

Q: How to **treat** if there is bleeding?

A: As follows:

- Drug should be stopped.
- Platelet count, PT, APTT and liver function tests should be done.
- Other causes of bleeding should be looked for.
- Symptomatic treatment should be given, may require blood transfusion.
- After improvement, drug should be started with low dose and then increase the dose (batch of the drug may be changed). If again bleeding, alternative drug may be given.

Q: What are the **complications** of kala-azar?

A: As follows:

- Secondary infection (pneumonia, tuberculosis).
- Anaemia.
- Bleeding.
- Gastroenteritis, bacillary dysentery.
- Liver disease (cirrhosis of liver).
- PKDL.
- Rarely, cancrum oris.

Causes of death in Kala-azar: If no treatment is given, patient may die within 1–2 year due to:

- Secondary infection.
- Bleeding.

Q: How to **treat** kala-azar?

A: As follows:

- Sodium stibogluconate: 20 mg/kg for 28 days IV or IM. Can be given in infusion with normal saline. IM injection is very painful, given if there is ECG abnormality (arrhythmia or long QT interval).
- Meglumine antimoniate: 50 mg/kg is an alternative.
- Liposomal amphotericin B: Drug of choice, 3–4 mg/kg daily, given on days 1–5, 14 and 21. May be repeated. Dose for immunoincompetent is 4 mg/kg on day 1–5, 10, 17, 24, 31 and 38. It is expensive and not widely available. Preferable to conventional amphotericin B, as it is more effective, less toxic, less protein bound, concentrated and retained in macrophage-rich organs (RE system) other than kidney (not nephrotoxic). Safe in pregnancy.
- Conventional amphotericin B: 1 mg/kg for 20 days, given in slow infusion for 4–6 h. It is more protein bound and nephrotoxic.
- New oral drug: Miltefosine, a cytotoxic drug, very effective and safe for visceral leishmaniasis. Also helpful in treating resistant kala-azar. Dose is 50–100 mg or 2.5 mg/kg daily orally for 28 days (50 mg, if < 25 kg body weight; and 100 mg, if > 25 kg body weight). Side effects are less, may cause vomiting, diarrhoea, transient rise of serum glutamic pyruvic transaminase (SGPT), blood urea nitrogen (BUN) and creatinine. It has more foetal toxicity; thus not recommended during pregnancy.
- Paromomycin: 11 mg/kg/day intramuscularly for 21 days.

N.B. Remember the following points while treating with sodium stibogluconate:

- Before starting the therapy, perform renal and hepatic function tests, ECG (to see

dysrhythmia, prolonged QT and ischaemia) and chest X-ray (latent TB, pneumonia).
- During IV injection, if the patient complains of chest pain or cough, stop the drug immediately.
- Monitor ECG, FBC including platelet, hepatic and renal functions.
- The drug should be stopped, if there is bleeding, ECG change (arrhythmia, prolonged corrected QT interval).
- No limitation of dose (previously it was thought that dose should not exceed 1 g/day).

Q: How to see the **response** of therapy?

A: As follows:
- Clinical improvement: Improvement of fever, feeling of well-being.
- Reduction in the size of spleen (may take months).
- Weight gain.
- Laboratory findings include increased Hb%, total count of WBC and increased albumin.

Q: What do you mean by **relapse, re-infection** and **resistant** kala-azar?

A: As follows:
- Relapse means after cure, there is again kala-azar usually within 6 months.
- Re-infection means after cure; there is again kala-azar after 6 months.
- Resistance means no response to drug therapy. It may be primary (no response from beginning of therapy) or secondary (develops later after initial response). It is usually due to insufficient or suboptimal dose or irregular therapy.

Q: How to **treat** if there is **relapse**?

A: Same therapy with sodium stibogluconate for double duration of initial treatment (56 days). Other drugs may be used.

Q: How to **treat** a resistant case of kala-azar?

A: In a resistant case of kala-azar, the following therapy should be given:
- Pentamidine isethionate. 3–4 mg/kg, three times per week for 5–25 weeks (at least 5 weeks and 15 injections should be given). Then, sodium stibogluconate 20 mg/kg for 30 days. Pentamidine may cause hypoglycaemia, hyperglycaemia and shock. It is not used as a first drug because of more side effects and development of quick resistance.
- Amphotericin B, preferably liposomal amphotericin B.
- Plus adjuvant therapy: γ-Interferon, allopurinol, ketoconazole.

Q: How to treat **kala-azar in pregnancy**?

A: Same treatment with sodium stibogluconate. Although the safety of this drug during pregnancy is not established, it should be treated since the disease is potentially dangerous.

Q: What is kala-azar treatment failure **(KATF)**?

A: When kala-azar does not respond to usual therapy with sodium stibogluconate, it is called KATF. It is usually due to inappropriate or suboptimal dose or irregular therapy. Treatment—as in resistant kala-azar.

Post-Kala-Azar Dermal Leishmaniasis (PKDL)

Presentation of a Case

- There are multiple, pale, pink, reddish, wart-like nodules of variable size and shape involving nose, cheek and ear lobule.
- Skin is thick.

My differential diagnoses are:
- PKDL.
- Lepromatous leprosy.
- SLE.
- Dermatomyositis.
- Sarcoidosis.
- MCTD.
- Neurofibromatosis.
- Others: Lipomatosis, acne rosacea, leukaemia cutis, secondary syphilis and rhinophyma (irregular thickening of skin of nose with enlarged follicular orifice).

Q: Ask **one question** to the patient.

A: Previous history of kala-azar.

Q: What is the more likely **diagnosis** in this case?

A: More likely diagnosis is PKDL.

Q: What is PKDL?

A: It is a nonulcerative, cutaneous lesion that occurs after successful treatment of visceral leishmaniasis. Initially starts as macules, then erythematous patches,

followed by wart-like nodular lesions on the face, ear lobules and limbs. Amastigotes are scanty in the lesion. After treatment, visceral infection disappears, but organisms may remain in skin. After a variable period, skin resistance is lost with resurgence of old infection, which leads to PKDL.

In India, it occurs in a small minority of patients 6 months to 3 years or more after the initial infection, creating a persistent human reservoir. They present as macules, papules, nodules (most common) and plaques on the face, mainly around the chin. The face is often erythematous. Hypopigmented macules can occur over all parts of the body, and are highly variable in extent and location. There are no systemic symptoms and no spontaneous healing.

In Sudan, about 50% develop skin manifestations of PKDL concurrently with visceral leishmaniasis or within 6 months afterwards. The skin features are as above. In addition, there may be a measles-like micropapular rash all over the body. Children are more frequently affected than in India. Spontaneous healing occurs in about three-fourth cases within 1 year.

Q: What is the **presentation** of PKDL?

A: As follows:

- Multiple, pale, pink, reddish, wart-like nodules of variable size and shape involving nose, cheek and ear lobule.
- Thick skin.

In early case, depigmented macules, erythematous, well-circumscribed lesions may be seen or all stages of lesions may be present, such as depigmented macules, erythematous lesions and nodules, or only multiple nodules of variable size and shape are seen.



Early PKDL (depigmented macules)



Early PKDL (few nodules)



PKDL (nodules)



PKDL (multiple nodules)

Q: What **investigation** is done to diagnose PKDL?

A: As follows:

- Demonstration of amastigote form of LD body in lesions by slit-skin smear and culture. Smear is prepared from nodular lesions (LD bodies are not found in depigmented lesion).

- Immunofluorescence and immunohistochemistry may demonstrate the parasite in skin tissue.
- In the majority of patients, serological tests (DAT or k39 strip tests) are positive. It is not helpful for diagnosis.

Q: How to treat PKDL?

A: As follows:

- In India, injection of sodium stibogluconate (given in cycles) 20 mg/kg daily for 20 days is given. After 10 days interval, the course is repeated. Total six cycles are needed with an interval of 10 days. Total 120 injections are needed.
- If a second course is required, it should be given after an interval of 2 months.
- In Sudan, same injection for 2 months is adequate.
- Alternatively, in India, several courses of amphotericin B infusions may be given.

N.B. Pentamidine is ineffective in PKDL.

Splenomegaly (Not Hepatomegaly)

Presentation of a Case

- The spleen is enlarged, ... cm from costal margin from anterior axillary line towards right iliac fossa.

Q: Why it is spleen, not kidney?

A: This is spleen because:

- The mass is in left hypochondrium.
- Moves with respiration downwards and towards right iliac fossa.
- I could not get above the swelling, and hand could not be insinuated between the mass and left lower rib.
- There is a notch (definitive sign).
- Percussion is dull over the mass and continuous up to the lower part of left side of chest.

Differences between spleen and kidney

Spleen	Kidney
It is in the left hypochondrium	It is in the lumbar region or loin
Moves with respiration towards right iliac fossa	Moves downward and forward
Well-defined medial border	Round in shape
Notch is present	Absent
Get above the swelling: Absent and finger cannot be insinuated between the mass and left costal margin	Present and finger can be insinuated between the mass and left costal margin
On percussion: Dullness over the mass, which is continuous with the left lower chest	Colonic resonance over the mass
Palpable	Ballotable

N.B. Remember the following points:

- Spleen must be enlarged at least 2–3 times of its usual size before it can be felt. Hence, once a spleen is palpable, it is definitely enlarged (always pathological).
- Enlarged spleen may be: Mild <4 cm, moderate 4–8 cm or huge > 8 cm.
- Spleen lies against posterolateral wall of abdominal cavity beneath 9th, 10th and 11th rib. Long axis of spleen lies along the 10th rib.
- Spleen enlarges towards the right iliac fossa. However, in children, spleen may be enlarged vertically towards the left iliac fossa.
- If kidney is hugely enlarged, colonic resonance may be absent and it may not be possible to get above the swelling.

Q: What are the causes of mass in left hypochondrium [differential diagnoses (DD) of splenomegaly]?

A: As follows:

- Splenomegaly.
- Enlarged left kidney.
- Mass in the splenic flexure of colon (carcinoma).
- Carcinoma of the stomach.
- Mass in the tail of the pancreas (carcinoma).
- Omental mass.

Q: What are the causes of splenomegaly?

A: Mention the causes according to the age of the patient:

If middle-aged or elderly, the causes are:

- Malaria.
- Kala-azar.
- CML.
- Myelofibrosis.
- Lymphoma.
- Cirrhosis of liver with portal hypertension
- Chronic lymphatic leukaemia.
- Tropical splenomegaly syndrome.

If young or of early age, the causes are:

- Malaria.
- Kala-azar.
- Hereditary haemolytic anaemia (β-thalassaemia major, HbE disease and hereditary spherocytosis).
- Lymphoma.
- Cirrhosis of liver with portal hypertension (causes are Wilson disease and α_1-antitrypsin deficiency).

Causes of huge splenomegaly (may cross the midline)

- Chronic kala-azar.
- Chronic malaria.
- CML.
- Myelofibrosis.
- Cirrhosis of liver with portal hypertension (occasionally, common in early age).
- Hairy cell leukaemia.
- Adult Gaucher disease.
- Rapidly progressive lymphoma.

Just-palpable spleen (spleen tip) found in (all the causes of huge splenomegaly in the early stage **plus** the following):

- Enteric fever.
- Subacute bacterial endocarditis (SBE).
- Viral infection (infectious mononucleosis and CMV infection).
- Collagen disease (SLE).
- Sarcoidosis.
- Polycythaemia rubra vera.

Q: What **relevants** do you want to see in a case of splenomegaly?

A: As follows:

- Lymph nodes (lymphoma, leukaemia, SLE and viral infection).
- In early age, anaemia, jaundice (hereditary haemolytic anaemia, also see frontal and parietal bossing, and mongoloid facies).
- Signs of CLD (see page 202).
- Heart to see murmur (SBE).
- Bony tenderness (for leukaemia).
- Pigmentation (for kala-azar).

Causes of lymphadenopathy with splenomegaly

- Lymphoma.
- Leukaemia [acute lymphoblastic leukaemia (ALL) and chronic lymphocytic leukaemia (CLL)].
- Viral infection (infectious mononucleosis, CMV infection and HIV).
- Collagen disease (SLE).
- Kala-azar (African kala-azar, also Chinese kala-azar).
- Others (sarcoidosis, brucellosis, toxoplasmosis and disseminated TB).

Causes of fever with splenomegaly

- Enteric fever.
- Malaria.
- Kala-azar.
- SBE.
- Viral infection (infectious mononucleosis and CMV infection).
- Lymphoma.
- Leukaemia.
- Collagen disease (SLE).
- Brucellosis.
- Toxoplasmosis.
- Disseminated TB.

Causes of splenomegaly with ascites

- Cirrhosis of liver with portal hypertension.
- Collagen disease (SLE).
- Lymphoma.
- Leukaemia.
- Disseminated TB.

Q: How **consistency** of spleen may help in diagnosis of splenomegaly?

A: It shows the following:

1. If the **spleen is soft**, causes may be:
 - Enteric fever.
 - SBE.
 - Viral infection.
 - Acute leukaemia.
2. If the **spleen is firm**, causes may be:
 - Cirrhosis of liver with portal hypertension.
 - CML.
3. If the **spleen is hard**, causes may be:
 - Malaria.
 - Kala-azar.

Q: What are the causes of **splenic atrophy** or **hyposplenism?**

A: Causes of atrophy or hyposplenism are:

- Sickle-cell disease (autosplenectomy due to repeated infarction in the second decade after 16 years of age).
- Coeliac disease.
- Dermatitis herpetiformis.
- Occasionally in inflammatory bowel disease (ulcerative colitis).
- Essential thrombocythaemia.

Q: What are the **risks of hyposplenism** or **splenectomy?**

A: After splenectomy:

- Increased risk of pneumococcal infection (patient should receive pneumococcal vaccine, 2–3 weeks before splenectomy).

- Meningococcal and *Haemophilus* infection.
- Malaria.

Q: What is the **blood picture** after splenectomy?

A: Blood pictures after splenectomy or hyposplenism:

- RBC shows Howell–Jolly body (nuclear remnants in RBC), target cell, acanthocytic cells (crenated or irregular RBC) and increased reticulocyte.
- WBCs initially, leucocytosis and increased neutrophil; it is normal after a few weeks. Later, increased lymphocytes and monocytes.
- Platelet increases immediately, normal in 1–2 months. In some cases, thrombocytosis may persist.

Q: What are the indications of **splenectomy**?

A: As follows:

- Hereditary spherocytosis.
- ITP (when there is failure of drugs).
- Autoimmune haemolytic anaemia (when there is failure of drugs).
- Huge splenomegaly with pressure symptoms.
- Hairy cell leukaemia.
- Rupture of spleen.
- Evidence of hypersplenism (suggested by repeated requirement of blood transfusion in a short interval).

Q: What is **hypersplenism**? What are the **causes**?

A: It is a syndrome characterized by:

- Splenomegaly.
- Reduction of one or more of blood cells (pancytopaenia).
- Increase cellularity of bone marrow.
- Improvement of blood picture after splenectomy.

Any cause of splenomegaly may cause hypersplenism, but is commonly found in:

- Haematological disease.
- Portal hypertension.
- Felty syndrome.
- Lymphoma.

Splenomegaly (Tropical Splenomegaly Syndrome)

Presentation of a Case

Present the cases as in splenomegaly (see page 187).

Mention tropical splenomegaly syndrome (TSS) as a cause of splenomegaly lastly, if asked.

Q: What is **tropical** splenomegaly syndrome?

A: In hyperendemic malarial area, there is gross splenomegaly associated with exaggerated immune response to repeated malarial infection called tropical splenomegaly syndrome (also called hyperreactive malarial splenomegaly; also previously it was called Banti syndrome). It is characterized by anaemia, massive splenomegaly and high IgM levels. Malarial parasites are scanty or absent.

Causes:

Aberrant immunological response to repeated infection by any of the species of malarial parasite. There is increased production of cytotoxic IgM antibody to CD8+ T lymphocytes, CD5+ T lymphocytes and increased ratio of CD4+ T cells: CD8+ T cells. In African patient, there is increase in lymphocytes (B-type) and may be confused with chronic lymphatic leukaemia.

Other features of TSS:

- Common in older children and adults. Splenomegaly is common; also hepatomegaly is common.
- There may be anaemia, pancytopaenia and evidence of hypersplenism.
- Acute haemolytic episode may occur; and portal hypertension may occur.

Cause of death: Due to infection. Respiratory and skin infections are common.

Diagnostic features of TSS:

- Hyperendemic area of malaria.
- Gross splenomegaly.
- Absent or low parasitaemia (no malarial parasite is found in peripheral blood or spleen).
- Increase in serum IgM.
- Malarial antibodies may be present in blood.
- Liver biopsy shows aggregates of IgM in Kupffer cells detected by immunofluorescence, sinusoidal lymphocytosis and hyperplasia.

Q: How to **diagnose** and **treat** TSS?

A: Diagnosis is done by exclusion of other diseases. Common investigations are:

- Full blood count (FBC) (anaemia, thrombocytopaenia and lymphocytosis).
- In bone marrow (lymphocytes infiltration).
- Liver biopsy shows Kupffer cells hyperplasia, lymphocytes infiltration and round-cell infiltration in portal tract. In some cases, fibrosis leading to portal hypertension.

Treatment:

1. In endemic area, chemoprophylaxis should be taken:
 - Proguanil 100 mg/day **plus** chloroquine 600 mg weekly.
 - Folic acid 5 mg/day.
2. In nonendemic area: Treatment of malaria.
 - Splenomegaly and anaemia usually resolve over a period of months with treatment. Long-term treatment may be necessary to prevent relapse.

Hepatomegaly

Presentation of a Case

- The liver is enlarged, ... cm from costal margin in the right midclavicular line.
- Margin is sharp (or rounded).
- Surface is smooth (or irregular).
- Tender (or nontender).
- Firm (or hard or soft in consistency).
- Upper border of liver dullness is in right, ... intercostal space (mention the location).
- There is (no or yes) hepatic bruit (or rub).

My diagnosis is **hepatomegaly**.

Q: Why it is liver?

A: Because:
- The mass is in right hypochondrium and in the epigastrium (left lobe).
- Moves with respiration.
- Get above the swelling—is not possible.
- Well-defined lower margin is parallel with the costal margin.
- Percussion is dull over it, which is continuous in lower part of chest.

Q: Can **liver be palpable** without hepatomegaly?

A: Yes, if it is pushed downwards by any pathology in the right side of chest, such as emphysema, pleural effusion or pneumothorax. It is normally palpable in neonate.

Q: What are the **causes** of hepatomegaly in this case?

A: Answer according to your findings and age of the patient.

1. **If huge hepatomegaly (firm or hard), the causes are:**
 - Hepatoma.
 - Secondaries in the liver.
 - Cirrhosis of liver (alcoholic cirrhosis, primary biliary cirrhosis and haemochromatosis).
 - CCF.
 - Polycystic liver.
 - Hydatid cyst.
 - Amyloidosis.
2. **If the liver is hard and nodular, the causes are:**
 - Hepatoma.
 - Secondaries in the liver.
 - Hydatid cyst.
 - Polycystic liver.
 - Others (amyloidosis, occasionally, cirrhosis of liver with macronodular).
3. **If firm hepatomegaly with irregular surface,** causes are:
 - Multiple secondaries.
 - Hydatid cyst.
 - Macronodular cirrhosis.
 - Granuloma (sarcoidosis).
 - Amyloidosis.
4. **If enlarged, tender liver, the causes are:**
 - Viral hepatitis.
 - Liver abscess (pyogenic or amoebic).
 - Congestive cardiac failure (CCF).
 - Chronic constrictive pericarditis.
 - Budd–Chiari syndrome.
 - Others (hepatoma and cholangiohepatitis).
5. **Causes** of **hepatomegaly** (soft or slightly firm with smooth surface, nontender):
 - Malaria.
 - Kala-azar.
 - Enteric fever.
 - Myeloproliferative disease (CML).
 - Lymphoproliferative disease (lymphoma, CLL and multiple myeloma).
 - Sarcoidosis.
6. Cause of enlargement of the **left lobe**:
 - Hepatoma.
 - Secondary in the liver.
 - Hydatid cyst.
 - Liver abscess (if tender).

Q: Why is it tender?

A: Due to stretching of Glisson capsule.

Q: What are the causes of **hepatic bruit?**

A: As follows:
- Hepatoma is the commonest cause (due to increased vascularity).
- Acute alcoholic hepatitis.

- AV fistula in liver (due to trauma or iatrogenic in liver biopsy).
- Haemangioma of the liver.

Q: What are the causes of **hepatic rub?**

A: As follows:

- Secondary deposit in the liver.
- Trauma.
- Infarction.
- Perihepatitis in pelvic inflammatory disease (gonococcal or chlamydial in females, called Fitz–Hugh–Curtis syndrome).

Q: What **else** do you want to see, if liver is enlarged and tender?

A: As follows:

- Jaundice (in viral hepatitis).
- Engorged and pulsatile neck veins, dependent oedema and to see heart (in CCF, chronic constrictive pericarditis).
- Tenderness and oedema in right lower chest (in liver abscess).

Q: What is the cause of **pulsatile liver?**

A: Tricuspid regurgitation (also vascular anomaly, AV fistula).

Q: What are the causes of **hepatomegaly in cardiac diseases?**

A: As follows:

- CCF.
- Pericardial effusion.
- Chronic constrictive pericarditis.
- Cardiomyopathy secondary to alcoholism, haemochromatosis, amyloidosis.

Q: What are the causes of **hepatomegaly associated with jaundice?**

A: As follows:

- Acute viral hepatitis.
- Weil disease.
- Haemolytic anaemia.
- Obstructive jaundice.

Q: Mention **one** investigation that is helpful for the diagnosis.

A: Ultrasonography of hepatobiliary system.

Q: What **investigations** do you suggest?

A: Investigations should be done according to the suspicion of cause:

1. USG of whole abdomen (first preferred test).
2. Complete blood count (CBC) (leucocytosis in pyogenic liver abscess).
3. If viral hepatitis is suspected, perform liver function tests (LFTs):
 - Serum bilirubin.
 - SGPT.
 - Alkaline phosphatase.
 - Viral markers for Hepatitis B virus (HBV) (HBsAg, HBeAg and anti-HBc), anti-HEV, anti-HCV and anti-HAV.
 - Prothrombin time.
4. If CLD is suspected:
 - Total protein, A:G ratio and prothrombin time (PT); also viral markers (for HBV and anti-HCV).
 - Endoscopy (to see oesophageal varices).
 - Proctoscopy (to see haemorrhoid in CLD).
 - CT or MRI.
 - Liver biopsy.
5. If hepatoma, then check for α-fetoprotein.

N.B. Normal liver edge may be just palpable; common in children. Other causes of normal palpable liver are emphysema, bronchial asthma and subphrenic abscess.

Q: How **liver biopsy** is done?

A: There are four methods:

- Percutaneous (by Vim–Silverman needle, Menghini needle or Tru-cut needle).
- Transjugular (if PT is prolonged and platelet count is low).
- Laparoscopy (if there is bleeding, it can be stopped easily through laparoscope).
- During laparotomy (if done for other reason).

Before liver biopsy, ensure the following points:

- Consent and cooperation of the patient.
- Exclude biliary obstruction, marked ascites, severe anaemia and high bilirubin.
- Prothrombin time should be normal (not more than 4 s that of control).
- Activated partial thromboplastin time (APTT) should be normal.
- Platelet count should not be <100,000/mm^3.

Follow-up after biopsy:

- The patient should be in complete bed rest for 24 h.
- Regular monitoring of pulse and BP.
- Blood should be kept ready for transfusion, if necessary.

N.B. If bilirubin is high, liver biopsy should not be done, as liver tissue does not take the stain.

Complications of liver biopsy:

- Bleeding.
- Pain (may radiate to shoulder).
- Rarely, biliary peritonitis and pneumothorax.

Q: What is liver span?

A: By percussion, upper border of liver dullness is in the sixth intercoastal space (ICS) or rib in right midclavicular line and the distance between this upper border and lower border is called liver span. Normally, it is less than 13 cm.

Hepatomegaly (Hepatoma)

Presentation of a Case

- The liver is enlarged, ... cm from the costal margin in right midclavicular line.
- Margin is irregular.
- Surface is irregular and nodular.
- Nontender.
- Hard in consistency.
- Upper border of liver dullness in ... intercostal space in right midclavicular line.
- There is hepatic bruit.

My differential diagnoses are:

- Hepatoma.
- Secondary deposit in liver.
- Others: Hydatid cyst and polycystic liver.

Q: Why is this hepatoma?

A: Because the liver is hard, irregular, nodular, nontender and there is hepatic bruit.

Q: Why not secondary deposit?

A: In secondary deposit, the nodules are usually multiple and small. There may be umbilication but no hepatic bruit. (There may be history of a primary carcinoma.)

Q: How to differentiate between primary carcinoma (hepatoma) and secondary carcinoma?

A: As follows:

Primary	Secondary
History of hepatitis B or C infection or cirrhosis of liver	History of primary carcinoma (GIT, bronchus, breast, thyroid and kidney); no primary source in 50% cases
Nodule usually single, may be more	Usually multiple nodules
No umbilication over the nodule	There is umbilication (due to necrosis)
Bruit present (due to increased vascularity)	No bruit (because of the necrotic lesion)
Rub may be present	Rub is more common
Investigations • α-fetoprotein increased • Alkaline phosphatase slightly increased • Carcinoembryonic antigen normal	Investigations • α-fetoprotein usually not increased • Alkaline phosphatase highly increased • Carcinoembryonic antigen increased

Q: How to suspect that hepatoma has developed in cirrhosis of liver?

A: In the following way:

- Rapid deterioration of general condition.
- Pain in right hypochondrium.
- Increasing ascites, not responding to usual therapy.
- Enlarging liver with appearance of nodule (hard and irregular).
- Presence of bruit.
- Biochemically increase α-fetoprotein.

Q: What are the causes of hepatoma?

A: As follows:

- Chronic hepatitis B infections. Hepaocellular carcinoma (HCC) is four times common in those with HBeAg positive than those with HBsAg alone. 75–90% are associated with cirrhosis of liver.
- Chronic hepatitis C infections. Risk of HCC is higher in hepatitis C virus (HCV) than HBV. Almost always associated with cirrhosis.
- Cirrhosis of liver: In alcoholic cirrhosis, nonalcoholic steatohepatitis (NASH), haemochromatosis, Wilson disease, α_1-antitrypsin deficiency and primary biliary cirrhosis. Macronodular variant is more prone to develop hepatoma.
- Aflatoxin produced by a fungus *Aspergillus flavus* (from contaminated ground nut grain stored in tropical condition).
- Chronic arsenicosis.
- Clonorchis sinensis (a parasitic infection).
- Prolonged androgen therapy, anabolic steroid and oral contraceptive pill (oestrogen) may cause hepatoma (usually adenoma, rarely hepatoma).
- Smoking (rare).

Q: What are the **screening tests** to detect hepatoma in cirrhosis of liver?

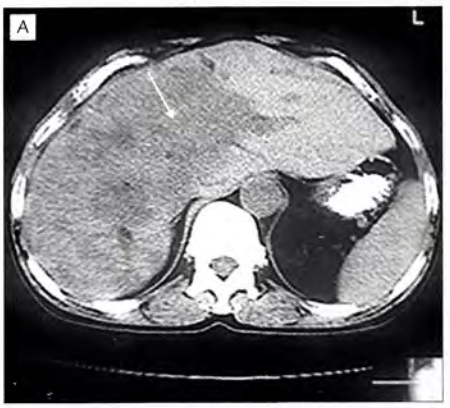
A: USG and α-fetoprotein are the screening tests. USG every 3–6 months in high-risk group to find out B and C infection, alcoholic cirrhosis and haemochromatosis.

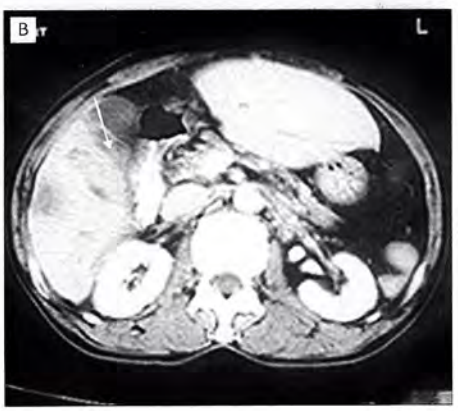
Q: What **investigations** are done to diagnose hepatoma?

A: As follows:

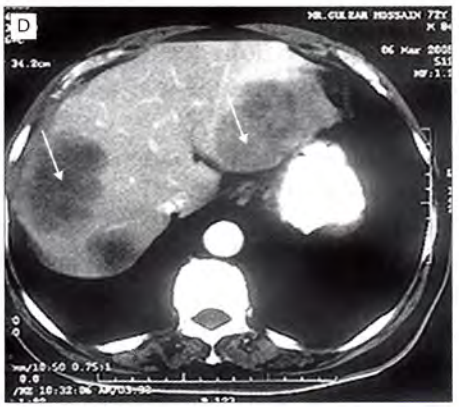
1. USG (shows filling defects in 90% of cases).
2. α-fetoprotein: High (60%), normal (one-third). Levels increase with the size of tumour.
3. Others:
 - CT or MRI.
 - Carcinoembryonic antigen (high in secondaries).
 - Plain X-ray of abdomen to see calcification in liver (sunburst calcification).
4. Liver biopsy under USG control. (This is confirmatory but avoided in patient eligible for transplantation or surgical resection because of small risk of tumour seeding along the needle tract).
5. Viral markers (HBV and HCV).

N.B. Metabolic abnormalities in hepatoma are polycythaemia, hypercalcaemia, hypoglycaemia and porphyria cutanea tarda.









CT scan of liver (hepatoma). (A, B) Hepatoma; (C, D) secondary deposit in liver

Q: What are the other **primary** tumours of liver?

A: Rarely, fibrolamellar hepatocellular carcinoma, common in young adults, affecting equally in male and female, in the absence of hepatitis B and cirrhosis. The tumour is large at presentation, α-fetoprotein is normal. This tumour is treated by surgical resection.

Other primary tumours include hemangioendothelial sarcoma, cholangiocarcinoma, hepatoblastoma, leiomyosarcoma, fibrosarcoma.

Q: What are the **benign tumours** of liver?

A: As follows:

- Haemangioma is the commonest. Rarely causes symptom. No treatment is required.
- Adenoma, more in females, caused by oestrogen containing oral contraceptives, androgen and anabolic steroid. Surgical resection, if pressure symptoms; also if pregnancy is desired (as size is increased in pregnancy).
- Focal nodular hyperplasia.
- Fibroma.
- Leiomyoma.

Q: Why **secondary carcinoma** is more common in the liver?

A: Because relatively blood flow in liver is more; double blood supply (by portal vein and hepatic artery).

Q: How to treat hepatoma?

A: As follows:

- Surgical resection in noncirrhotic patient. Recurrence is 50% at 5 years.
- In cirrhotic patient, resection may be done with small tumour and good liver function.
- Liver transplantation (5 year survival is 70% with single tumour <5 cm, or three tumours <3 cm). Hepatitis B and C may recur in transplanted liver.
- Percutaneous injection of ethanol, if tumour size is 3 cm or less, 80% cure rate. Recurrence is 50% at 3 years. Repeated injection may be given. It causes tumour necrosis.
- Transcatheter radiofrequency ablation using a single electrode inserted into the tumour under radiological guidance.
- Transcatheter hepatic arterial embolization [transarterial chemoembolization (TACE)] by Gelfoam and doxorubicin. TACE is contraindicated in decompensated cirrhosis and multifocal HCC.
- Chemotherapy: Doxorubicin may be effective in 30% cases. Sorafenib IV, a multikinase inhibitor, is under phase III trial.

Q: What is α-fetoprotein? What are the causes of high α-fetoprotein?

A: It is a normal component of plasma protein, produced by the foetal liver older than 6 weeks and reaches maximum concentration at 12–16 weeks of fetal life. It falls few weeks after birth. Reappearance in blood in adult life is pathognomonic. Causes of high α-fetoprotein:

1. Hepatoma is the commonest, may be very high, >500 ng/mL in patients with liver disease is highly suggestive. Level increases with size, may be normal in small size.
2. Others:
 - Chronic active hepatitis (indicates hepatocellular regeneration).
 - Acute viral hepatitis (indicates hepatocellular regeneration).
 - Acute hepatic necrosis following paracetamol toxicity.
 - Embryonic tumours of the ovary and testis.
 - Embryonic hepatoblastoma.
 - Rarely, in other malignancy-like carcinoma of stomach, pancreas, bile duct and gall bladder (usually with large metastasis in liver).
 - During pregnancy (in serum and amniotic fluid), high level indicates neural tube defect (meningomyelocele or anencephaly).

Fitz–Hugh–Curtis Syndrome

Fitz–Hugh–Curtis syndrome is caused by *Chlamydia* or *Gonococcus* infection, which tracks up the right paracolic gutter to cause perihepatitis, secondarily from endocervical or urethral infection. It is characterized by fever, pain in the right hypochondrium with radiation to right shoulder, tender hepatomegaly, hepatic rub and small right pleural effusion, and so on. (*Chlamydia* infection is asymptomatic in 80% cases.) Investigation shows endocervical swab for microscopy and special culture, direct fluorescent antibody for *Chlamydia*, ELISA and PCR may be performed.

Treatment: Tetracycline or doxycycline or erythromycin or azithromycin are used for *Chlamydia* infection.

Ascites with Splenomegaly (Tuberculous Peritonitis)

Presentation of a Case

- The patient has ascites with splenomegaly.

My differential diagnoses are (causes of splenomegaly with ascites):

- Cirrhosis of liver with portal hypertension.
- Lymphoma.
- SLE.
- Disseminated TB.
- Leukaemia.



Huge ascites

Q: How to diagnose **tuberculous peritonitis?**

A: As follows:

1. History:
 - History of pulmonary tuberculosis.
 - General features of tuberculosis like low-grade fever, mainly evening rise, weight loss, sweating.
 - Abdominal pain, diarrhoea or features of intestinal obstruction.
2. Physical examination:
 - Abdomen is doughy.
 - Mass in right iliac fossa (ileocaecal TB).
3. Investigation:
 - CBC, ESR.
 - MT (positive in 50% cases).
 - Chest X-ray (may be primary focus in 50% cases).
 - USG of abdomen, CT scan of abdomen.
 - Ascitic fluid study:
 - Straw colour.
 - High protein >25 g/L (exudative), low glucose.
 - High lymphocyte.
 - Adenosine deaminase (ADA) is high.
 - Acid-fast bacilli (AFB) are rarely found. Mycobacteria culture and sensitivity may be positive for up to 50% cases.
 - PCR of ascitic fluid.
 - Laparoscopy: Tubercle may be seen over the peritoneal and omental surface (biopsy should be taken).

Q: What is the commonest site of abdominal tuberculosis?

A: Ileocaecal region. (Peritoneum is the second common site.)

Q: What are the **types** of tuberculous peritonitis?

A: Three subgroups:

- Wet type: In such case, ascitic fluid protein is >20 gm/L; tubercle bacilli are rarely found.
- Dry type: In such case, patient presents with subacute intestinal obstruction, which is due to tubercular small bowel adhesion.
- Fibrous type: In such case, patient presents with abdominal pain, distention and ill-defined irregular tender abdominal mass.

Q: What is the **feeling** of abdomen on palpation in tuberculous peritonitis?

A: Doughy feeling.

Q: How to **treat?**

A: As follows:

- Standard anti-TB drugs for 1 year.
- Surgery in some cases (if fistula or obstruction).
- Symptomatic treatment for pain and diarrhoea.
- Prednisolone in some cases.

Hepatomegaly (Tender Liver, Viral Hepatitis)

Presentation of a Case

- Liver is enlarged, ... cm from the costal margin in right midclavicular line.
- Margin is sharp, surface is smooth, tender, soft in consistency, upper border of liver dullness is in right, ... intercostal space (mention location) and no hepatic bruit or rub.

My diagnosis is **tender hepatomegaly,** which may be due to:

- Acute viral hepatitis.
- Liver abscess.
- CCF.
- Chronic constrictive pericarditis.
- Weil disease

Q: If it is viral hepatitis, what **else** do you want to see?

A: Jaundice.

Q: What **history** do you like to take in viral hepatitis?

A: As follows:

1. Anorexia, nausea and vomiting.
2. Pain (usually in right hypochondrium).
3. High-coloured urine, yellow eye and body.
4. Itching, pale stool (due to intrahepatic cholestasis).
5. History of (for HBV):
 - Injection or infusion of blood and blood products, any fluid.
 - Injection of contaminated needle or sharing of syringe by others or parenteral drug abusers.
 - Close contact with infected person.
 - Newborn in infected mother with HBV.
 - Acupuncture or tattooing.
 - Homosexuality.
 - Organ transplantation.
 - Chronic haemodialysis.
 - Travel to other parts.
 - Newborn in infected mother with HBV.

N.B. Clinical features and pathological features are same by all viruses. They differ in their tendency to cause acute and chronic infections. HBV and HCV may cause chronic hepatitis; hepatitis D virus (HDV) can cause chronic infection with HBV. HAV and hepatitis E virus (HEV) are not associated with chronic infection.

Q: What **investigations** do you suggest in acute viral hepatitis?

A: As follows:

1. CBC (there may be leucopaenia, with relative lymphocytosis).
2. LFTs:
 - Serum bilirubin: High.
 - SGPT: High.
 - Serum glutamic oxaloacetic transaminase (SGOT): May be high (SGOT is raised in drug-induced hepatitis).
 - Alkaline phosphatase may be high (rarely more than twice the upper limit. In cholestatic hepatitis, alkaline phosphatase may be very high).
 - Prothrombin time: Prolonged in severe hepatitis.
3. Viral markers:
 - Virus A (anti-HAV, IgM indicates acute infection).
 - Virus B (HBsAg, HBeAg, anti-HBc). In acute infection, HBsAg may be cleared rapidly; anti-HBc IgM is diagnostic.
 - Virus E (anti-HEV, IgM indicates acute infection), anti-HCV.
4. USG of hepatobiliary system.
5. Others: Blood sugar, urine routine examination (R/E).

N.B. Remember the following points:

- HBsAg appears in the blood 6 weeks to 3 months after acute infection, then disappears.
- HBeAg rises early and declines rapidly.
- Anti-HBc is the first antibody to appear and high titers of IgM anti-HBc suggest acute infection and continuing viral replication. It persists for many months.
- Anti-HBsAg appears late and indicates immunity.
- Anti-HBe appears after anti-HBc. Its appearance indicates decreased infectivity.

Q: What are the **markers** of HBV infection?

A: As follows:

- HbsAg.
- HbeAg (indicates active replication; if persists for >6 months, it indicates chronic infection).
- Anti-Hbc (IgM type indicates acute infection).
- HBV DNA.

Q: What are the **markers** of B virus replication?

A: HbeAg, HBV DNA.

Q: What are the causes of **acute hepatitis**?

A: As follows:

- Acute viral hepatitis (see below).
- Drugs: Paracetamol, alcohol.
- Nonviral infection: *Toxoplamsa gondii, Leptospira icterohaemorrhagiae, Coxiella burnetii* (Q fever).
- Others: Pregnancy, Wilson disease, poisons (amanita phyllodes mushroom, aflatoxin, carbon tetrachloride).

Q: What are the **viruses** causing hepatitis?

A: As follows:

- Hepatitis A, B, C, D and E virus.
- Other viruses are Epstein–Barr virus, CMV, herpes simplex virus and yellow fever virus.

N.B. **Hepatitis** D virus is a RNA-defective virus can infect only with B virus or can superinfect in those who are HBV carriers. Only B virus is DNA type, and all others are RNA type.

Q: What are the causes of **chronic hepatitis**?

A: As follows:

- Virus: HBV, HCV and combined HBV and HDV.
- Autoimmune.
- Drugs: Methyldopa, isoniazid, ketoconazole, nitrofurantoin.
- Alcohol.
- Hereditary: Wilson disease, haemochromatosis, α_1-antitrypsin deficiency.
- Inflammatory bowel disease (ulcerative colitis).

Q: How would you **treat** a patient with acute viral hepatitis?

A: As follows:

- Bed rest.
- Normal diet.
- Supportive and symptomatic.
- Avoid sedative, opium and alcohol.

Q: What is the **prognosis** of acute viral hepatitis?

A: It depends on the type of the virus:

1. HAV:
 - Good, recovery in 3–6 weeks.
 - Rarely (0.1%) develop acute liver failure.
 - Mortality in young adult is 0.1% from acute fulminating hepatic failure. Mortality increases with age.

2. HBV:
 - In 90–95% cases, full recovery occurs within 6 months.
 - 5–10% develop chronic infection, which usually continues for life. Many may remain as inactive HBV infection. In some, cirrhosis of the lever and hepatoma may develop after many years. Cirrhosis usually develops in 5–20% cases in 5–20 years. This proportion is higher in those with e-antigen positive.
 - <1% may develop fulminating liver failure.
 - Infection from mother to child during pregnancy leads to chronic infection in child in 90% cases and recovery is rare.
 - Chronic infection is also common in Down syndrome and HIV infection.
3. HCV:
 - Rarely causes acute infection.
 - Commonly, it causes chronic hepatitis.
4. Combined HBV and HDV infection can cause more aggressive disease.
5. HEV:
 - Similar to HAV.
 - Can cause acute liver failure with high mortality in pregnancy.

Q: What are the **complications** of acute viral hepatitis?

A: As follows:

- Acute fulminating hepatic failure (by B and sometimes with E viral infection in pregnancy. It is rare by HAV).
- Relapsing hepatitis, which may be clinically evident (5–15%) or, more commonly, only biochemically detectable. It settles spontaneously.
- Cholestatic hepatitis mostly by HAV; may persist for 7–20 weeks.
- Posthepatitis syndrome is seen in anxious patient who complains of malaise, anorexia, nausea, vomiting, right hypochondrial pain or discomfort in the absence of clinical or biochemical evidence of liver disease. Reassurance is necessary.
- CLD (due to B and C virus), which may lead to cirrhosis of liver and ultimately to hepatoma.
- Others: Aplastic anaemia (usually reversible), rarely Coombs positive haemolytic anaemia, polyarteritis nodosa, Henoch–Schönlein purpura, glomerulonephritis and collagen vascular disease.

Brief Discussion on Weil Disease (Leptospirosis)

Q: What is **Weil disease?** What is its mode of infection, clinical features, investigation and treatment?

A: It is a leptospiral disease caused by *Leptospira icterohaemorrhagiae* characterized by high fever, jaundice, haemorrhage and renal impairment.

Mode of infection: Spread is typically by contact with infected rat urine.

Incubation period: 7–14 days.

Clinical features: There are two phases:

1. Leptospiraemic or bacteremic phase: This phase lasts for 1 week. Organisms may be found in blood and CSF. Characterized by:
 - High fever with chill.
 - Anorexia, nausea, vomiting.
 - Headache, myalgia (mainly calf and back).
 - Conjunctival suffusion (blood-shot eyes).
 - Skin rash (maculopapular, purpura, bruise, etc.).
 - Lymphadenopathy.
 - Jaundice, hepatosplenomegaly.
 - In severe case, renal impairment (caused by impaired renal perfusion and acute tubular necrosis, manifested as oliguria or anuria) and haemorrhage (epistaxis, haematemesis, melaena, etc.) may occur. There may be liver failure, myocarditis, pulmonary haemorrhage, encephalitis, aseptic meningitis may occur. There may be cardiac failure, haemolytic anaemia, thrombocytopaenia.
 - Relative bradycardia, neck rigidity may be found.
2. Immunological phase: There is development of antibody and leptospira disappears from blood. It lasts for 2–5 days. Features are usually mild, but meningism or aseptic meningitis and iridocyclitis may occur. Majority recover uneventfully.

N.B. Any patient with high fever, jaundice, bleeding manifestations and renal involvement; Weil disease is a strong possibility.

Organism and animal hosts:

- *Leptospira icterohaemorrhagiae* of rat.
- *Leptospira pomona* of pig.
- *Leptospira canicola* of dog.
- *Leptospira hardjo* of cattle.

Investigations:

- CBC: Usually polymorphonuclear leucocytosis; thrombocytopaenia in severe case.
- Blood culture (Fletcher media): Positive in first week of illness (within 4 days of illness).
- Urine R/E: Proteinuria, haematuria, RBC cast.
- Urine culture for leptospira in second week.
- LFT: High bilirubin, SGPT and PT.
- Serum CPK is high.
- Serological test: Microscopic agglutination test (MAT) positive at the end of first week. ELISA, immunofluorescence technique, etc. may be done.
- CSF study: Abnormal in 90% cases.
- PCR: Leptospira DNA by PCR in blood can be detected in early symptomatic disease and also in urine from eighth day of illness; may remain for months thereafter.

Treatment:

1. Antibiotic:
 - IV benzyl penicillin (1.5 million units 6 hourly for 1 week) or ampicillin (1 g 6 hourly for 1 week). Ceftriaxone (1 g daily for 1 week) is as effective as penicillin.
 - Doxycycline (100 mg 12 hourly for 1 week) or ampicillin (750 mg 6 hourly for 1 week) when started within 4 days of onset of symptoms.
2. In renal failure and jaundice:
 - Fluid and electrolyte balance must be maintained.
 - Dialysis may be needed.
 - Exchange transfusion may be needed in severe hyperbilirubinaemia.
3. If anaemia and thrombocytopaenia: Blood transfusion may be needed.

Prophylaxis: Doxycycline 200 mg weekly may have a role.

Hepatomegaly (Liver Abscess)

Presentation of a Case

Present as in viral hepatitis.

My diagnosis is **tender hepatomegaly,** which may be due to:

- Acute viral hepatitis.
- Liver abscess.
- CCF.
- Chronic constrictive pericarditis.
- Weil disease

Q: What **else** do you like to see in liver abscess?

A: As follows:

- Local oedema and fullness of intercostal space (in right lower chest).
- Local intercostal tenderness (right lower chest) called punch tenderness.
- Patient may have high temperature and looks toxic.

Q: What are the **types** of liver abscess?

A: They are of two types:

- Pyogenic liver abscess.
- Amoebic liver abscess.

Q: What are the **causes of pyogenic** liver abscess? What are the **causal organisms?**

A: As follows:

- Ascending cholangitis in biliary obstruction (common bile duct) by stone, stricture and neoplasm, or spreads from empyema of gall bladder.
- Haematogenous:
 - Portal pyaemia (mesenteric infection) from intra-abdominal sepsis, suppurative appendicitis and perforation.
 - Septicaemia or bacteraemia (along the hepatic artery).
- Direct extension from peripheral abscess.
- Trauma.
- Infection of liver tumour or cyst.

Causal organisms are *Escherichia coli, Streptococcus milleri, Streptococcus faecalis* or other *Streptococcus* species, *Staphylococcus aureus, Proteus vulgaris,* anaerobic organisms or bacteroids (from large bowel). Often the infection is mixed.

Q: How does the patient usually **present?**

A: As follows:

Pyogenic liver abscess:

- Fever, may be high with chill and rigour, malaise, anorexia and weight loss.
- Abdominal pain, mainly in right upper abdomen, may radiate to right shoulder.
- Pleuritic right lower chest pain (may be small pleural effusion, pleural rub).
- Jaundice is usually mild, may be severe in multiple abscesses causing biliary obstruction.
- Sometimes, only pyrexia of unknown origin (PUO) may be present.

N.B. Single abscess is common in right lobe; multiple abscesses are due to infection secondary to biliary obstruction. Immunocompromised patients are likely to develop liver abscess. Complications include rupture, secondary infection and septicaemia.

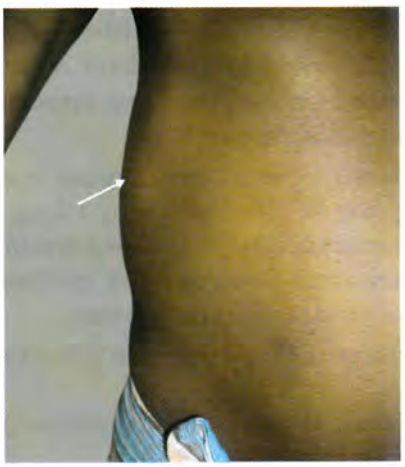
Amoebic liver abscess (common in right lobe, usually single):

- History of diarrhoea or intestinal disease (absent in 50% cases).
- Fever (low grade) and pain.
- Toxicity is absent.

N.B. Amoebic liver abscess is usually large, single and located in right lobe. Multiple abscesses may occur in advanced disease.



Liver abscess (fullness of intercostal space)



Liver abscess (swelling in right lower chest)

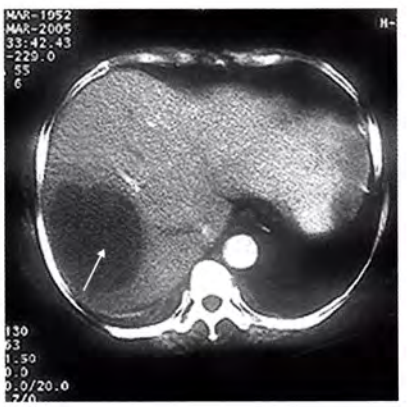
Q: What is the **character of pus** in amoebic liver abscess?
A: Pus is in chocolate or anchovy sauce colour.

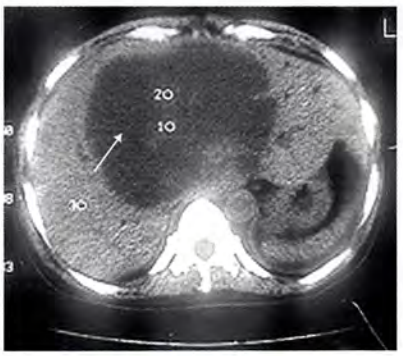
Q: What are the **differences** between pyogenic and amoebic liver abscess?
A: As follows:

Points	Pyogenic	Amoebic
Organism	*Escherichia coli* and others	*Escherichia histolytica*
History	Cholangitis, septicaemia	Amoebiasis
Symptoms	High fever with chill and rigour	Fever mild-to-moderate, no chill and rigour
Neutrophil leucocytosis	Common	Less
Ultrasonography	Multiple lesions	Usually single
Aspiration	Frank pus	Chocolate or anchovy sauce
Prognosis	More fatal	Less fatal

Q: What **investigations** do you suggest in liver abscess?
A: As follows:

1. FBC (leucocytosis in pyogenic liver abscess).
2. LFT (usually high alkaline phosphatase; bilirubin is high in 25% cases. Aminotransferases are usually normal, may be slightly high).
3. Serum albumin (low), a fetoprotein.
4. Chest X-ray (PA view) shows raised right dome of diaphragm, small right-sided pleural effusion or collapse of right lung.
5. Blood for culture and sensitivity (C/S) (in pyogenic, positive in 30% cases. In some series, 50–80% cases may be positive).
6. USG of the upper abdomen.
7. CT scan (shows multiple bull's-eye appearance) or MRI of the upper abdomen may be done.
8. If needed, USG-guided aspiration of pus for C/S (in pyogenic), and amoebae is rarely found in pus.
9. For amoebic liver abscess:
 - Immunofluorescent antibody test (positive in 95%).
 - Indirect haemagglutination test (positive in 95%).
 - Complement fixation test.
 - ELISA.





Liver abscess (A and B)

Q: How to treat liver abscess?

A: As follows:

1. Pyogenic liver abscess:
 - Antibiotic (amoxicillin plus gentamicin) **plus** metronidazole. Cefoperazone (1–2 g IV 12 hourly) with metronidazole (500 mg every 6 h) is an alternative. To be continued for 2–3 weeks, sometimes up to 6 weeks.
 - If larger (>5 cm) liver abscess or not responding to antibiotic therapy, then USG-guided aspiration should be done.
 - Surgical drainage is rarely needed. Even more rarely hepatic resection may be indicated for chronic persistent abscess or pseudotumour.
 - Treatment of the underlying cause like biliary obstruction.
2. Amoebic liver abscess:
 - Metronidazole 800 mg 8 hourly for 10 days, or secnidazole 2 g daily for 5 days, or tinidazole or ornidazole 2 g daily for 3 days.
 - Nitazoxanide 500 mg 12 hourly for 3 days.
 - Diloxanide furoate 500 mg 8 hourly for 10 days or paromomycin should be given for intestinal infection. This is given after the treatment of amoebic liver abscess.
 - USG-guided aspiration should be done if abscess size is large (>5 cm), there is no response to medical therapy or if there is a risk of bursting.

N.B. Remember the following points:

- Mixed infections may be found in many cases. Hence, antibiotic plus antiamoebic drugs may be needed.
- Abscess may rupture into pleural cavity, pericardial sac or peritoneal cavity. In such cases, immediate aspiration or surgical drainage is needed.

Hepatomegaly (Hydatid Cyst)

Presentation of a Case

- The liver is enlarged, ... cm from the costal margin in right midclavicular line.
- Margin is rounded.
- Surface is nodular.
- Nontender.
- Hard in consistency.
- Upper border of liver dullness in ... intercostal space in right midclavicular line.
- There is no hepatic bruit.

My differential diagnoses are:

- Hepatoma.
- Secondary deposit in liver.
- Hydatid cyst.
- Polycystic liver.
- Cirrhosis of liver (macronodular).

Q: How does the patient **present** with hydatid cyst of liver?

A: As follows:

- Usually asymptomatic.
- Mass in right hypochondrium.
- Occasionally, jaundice due to obstruction in bile duct.
- Rarely rupture into the abdominal cavity; pleural cavity or biliary tree may occur. If it ruptures into the biliary tree, there may be intermittent jaundice, abdominal pain and fever. A cyst rupturing into the bronchus may cause expectoration and spontaneous cure.
- Features of cyst in other organs: A cyst in the lung may be infected causing a lung abscess or pulmonary abscess. If there is a cyst in the brain, it may cause seizure. Renal involvement may cause haematuria or lumbar pain.
- Calcification of cyst occurs in 40% of cases.

Q: What are the **complications** of hydatid cyst?

A: As follows:

- Pressure effect to the surrounding tissue.
- Rupture (abdominal or pleural cavity, biliary tree); may cause anaphylactic shock.
- Secondary infection.

Q: What are the **sites** of hydatid cyst?

A: As follows:

- Liver: 60%, usually right lobe (liver is the first filter).
- Lungs: 30% (it is the second filter).
- Kidneys: 3%.
- Brain: 1%.
- Any organ (spleen, heart, muscles and biliary tree).

Q: How human is **infected** by hydatid cyst?

A: Close contact with infected dog, or eating undercooked vegetables or drinking water contaminated with faeces of infected dog. Infection commonly occurs during childhood. After ingestion of the eggs, the embryo in liberated from the ovum in the small intestine and gains access to the blood stream and is carried to other organs. A slowly growing thick-walled cyst is formed, inside which further larval stage of the parasite develops.

Q: Who are the **definitive** and **intermediate** hosts?

A: As follows:

- Definitive host: Dogs (common) and other canine animals (fox, wolf and jackal).
- Intermediate host: Sheep (common), pig, cattle, goat and man.

Q: What are the **organisms** of hydatid cyst?

A: As follows:

- *Echinococcus granulosus* of dogs.
- *Echinococcus multilocularis* life-cycle between fox and vole. Man is infected accidentally.

Q: How are **dogs** infected?

A: By eating infected meat of sheep, pig, cow, etc. These animals are infected while grazing in the field contaminated with dog's faeces.

Q: What **investigations** do you suggest?

A: As follows:

- CBC (high eosinophils).
- USG and CT scan: Shows cyst and also daughter cysts within the parent cyst.
- Serology by performing complement fixation test (CFT) (positive in 70–80% cases), haemagglutination test (positive in 85%), flocculation test, indirect fluorescent antibody test, immunoelectrophoresis test (Arc5-test) and ELISA (positive in 70–90% cases).
- Plain abdomen X-ray (calcification may be seen).
- Casoni test (nonspecific): It is done by intradermal injection of 0.2 mL hydatid fluid in forearm (a control with normal saline in other arm). In positive cases, there is formation of wheal with pseudopodia in 20–30 min (it disappears in 1 h).



Hydatid cyst in liver



Simple cyst in liver

Q: How to **treat** hydatid cyst?

A: As follows:

1. Surgical treatment: Cyst should be removed, if possible, after first sterilizing the cyst with alcohol, 2.7% NaCl or 0.5% silver nitrate. Praziquantel 20 mg/kg for 14 days kills protoscolices perioperatively.
2. Medical treatment:
 - Albendazole 15 mg/kg in two divided doses for 12 weeks to 6 months. May be repeated (it cures in 30% and provides symptomatic relief in 50% cases).
 - Mebendazole 400 mg twice daily for 12 weeks to 6 months; may be repeated.
3. PAIR therapy (Puncture, Aspiration, Injection and Re-aspiration): Percutaneous aspiration of cyst, followed by injection of 100% ethanol into the cyst, then re-aspiration of cyst contents. Mebendazole may be combined with PAIR.
4. Calcified cyst may be left untreated.

Chronic Liver Disease or Cirrhosis of Liver

(May be isolated splenomegaly, hepatomegaly, or hepatosplenomegaly or ascites.)

Presentation of a Case

- There is generalized distension of abdomen, flanks are full and umbilicus is everted.
- Shifting dullness is present.
- Fluid thrill is present (mention if any).
- Spleen is enlarged, 2 cm from the left costal margin in anterior axillary line towards the right iliac fossa.

My diagnosis is ascites with splenomegaly, which is more likely due to cirrhosis of the liver with portal hypertension.

Q: What are the causes of **splenomegaly with ascites?**

A: As follows:

- Cirrhosis of liver with portal hypertension.
- Collagen disease (SLE).
- Lymphoma.
- Leukaemia.
- Disseminated TB.

Q: What **else** do you like to see?

A: I want to see the stigmata of CLD, lymph node in other areas, skin rash, mouth ulcer, joints (SLE).

Q: What are the **stigmata** or **signs** of CLD?

A: As follows:

1. Hands:
 - Palmar erythema (liver palm).
 - Dupuytren contracture.
 - Leuconychia.
 - Clubbing.
 - Flapping tremor.
 - Others include scratch marks, spider angioma, xanthoma, pigmentation, jaundice and cyanosis.
2. Face:
 - Parotid enlargement (bilateral).
 - Xanthelasma.
 - Spider angioma (also in neck, arm, forearm, hand and any part above the nipple line).
 - Pigmentation.
 - Hepatic facies.
 - Jaundice.
 - Cyanosis.
3. Chest:
 - Gynaecomastia (also spider angioma).
 - Less hair in chest or body, scanty axillary (also pubic hair).
 - Engorged veins in chest and also abdomen (due to portal hypertension).
4. Others:
 - Abdomen with splenomegaly, ascites, engorged veins and caput medusae.
 - Testis is small and atrophied.
 - Generalized pigmentation (any CLD can cause pigmentation, but commonly in haemochromatosis and primary biliary cirrhosis).
 - Purpura and ecchymosis.

Q: What **specific findings** will you see in CLD or cirrhosis of liver in a **young** patient?

A: As follows:

- The eyes should be examined to see **Kayser–Fleischer** (KF) ring for Wilson disease.
- In lung, signs of emphysema may be present in case of α_1-antitrypsin deficiency.

Common signs in alcoholic cirrhosis:

- Bilateral parotid enlargement.
- Florid spider angioma.
- Dupuytren contracture.
- Gynaecomastia.
- Testicular atrophy with loss of body hair.

Q: What is chronic liver disease **(CLD)** and **chronic liver failure?**

A: As follows:

- CLD is defined as liver disease for 6 months or longer.
- Chronic liver failure means functional capacity of liver cannot be maintained, and is characterized by encephalopathy and/or ascites. When chronic liver failure occurs, it is called decompensated liver disease.

Q: What is **cirrhosis** of liver? What are the **types?**

A: Cirrhosis of liver is a chronic diffuse liver disease characterized by destruction of liver cells with fibrosis, distortion of normal liver architecture and nodular regeneration due to proliferation of surviving hepatocytes. The **three types** of cirrhosis are:

- Micronodular: Regenerative nodule is usually small of 1-mm size, involving every lobule, also called Laennec cirrhosis, and is common in alcoholics.
- Macronodular: Large nodules, common in post-necrotic cirrhosis, found in HBV.
- Rarely, mixed type (micronodular and macronodular).

Q: What are the **signs** of portal hypertension?

A: As follows:

- Splenomegaly (single definite sign, mild in adult but marked splenomegaly in childhood and adolescent). Hypersplenism is common (pancytopaenia).
- Ascites.
- Collateral circulation, oesophageal varices, haemorrhoid and venous hum (between xiphisternum and umbilicus called Cruveilhier–Baumgarten syndrome).
- Portosystemic encephalopathy.
- Endoscopy shows oesophageal varices.

N.B. Remember the following points:

- Normal portal pressure, 2–5 mmHg. If >12 mmHg, then it is a sign that symptoms and complications might develop.
- Portal vein is formed by fusion of superior mesenteric vein and splenic vein.
- In adults, cirrhosis of liver is the common cause of portal hypertension.
- In children, extrahepatic portal vein obstruction is the common cause.

Q: What are the **causes** of cirrhosis of liver?

A: As follows:

- Chronic viral hepatitis (B or C, or B and D).
- Chronic alcoholism.
- Nonalcoholic fatty liver disease (NAFLD).
- Immunological (autoimmune liver disease and primary sclerosing cholangitis).
- Biliary [primary biliary cirrhosis (PBC), secondary biliary cirrhosis and cystic fibrosis].
- Genetic (haemochromatosis, Wilson disease and α_1-antitrypsin deficiency).
- Budd–Chiari syndrome.
- Drugs: Methotrexate.
- Idiopathic or cryptogenic.

Q: What are the **commonest causes** of cirrhosis of liver?

A: Viral infection (B and C), alcohol, NAFLD. In young patient with cirrhosis, Wilson disease may be an important cause.

Q: What are the **signs of decompensated cirrhosis**?

A: As follows:

- Ascites.
- Increasing jaundice.
- Hepatic encephalopathy.
- Portal hypertension with variceal bleeding.
- Worsening liver function (prolonged PT and low albumin).

Q: What are the **complications** of cirrhosis of liver?

A: As follows:

- Portal hypertension with rupture of oesophageal varices (haematemesis and melaena).
- Portosystemic encephalopathy (hepatic precoma) and hepatic coma.
- Hepatorenal syndrome.
- Hepatopulmonary syndrome.
- Hepatoma.
- Spontaneous bacterial peritonitis (SBP).

Q: What is the **mechanism of ascites** in cirrhosis of liver?

A: It is mainly due to renal reabsorption of sodium and water. Multiple factors are involved, such as:

1. Splanchnic vasodilatation is the main factor for ascites in cirrhosis of liver. This is mediated by vasodilators (mainly nitric oxide) that are released when the portal hypertension causes shunting of blood into the systemic circulation. Due to splanchnic vasodilatation, systemic arterial pressure falls, which leads to activation of renin–angiotensin mechanism with secondary aldosteronism, increased sympathetic activity, increased atrial natriuretic peptide secretion and altered activity of kallikrein–kinin system. All these produce salt and water retention.
2. Other factors are:
 - Combination of splanchnic vasodilatation and portal hypertension alters intestinal capillary permeability, leading to accumulation of fluid in peritoneal cavity.
 - Portal hypertension also increases local hydrostatic pressure and causes increased hepatic lymph production, which accumulates into the peritoneal cavity.
 - Low albumin causes low plasma osmotic pressure, which causes extravasation of fluid.
 - Failure to metabolize vasopressin by the liver that causes further retention of fluid.

Q: How to **treat** ascites in cirrhosis of liver?

A: As follows:

1. Bed rest. It improves renal flow (in horizontal position) and increases diuresis.
2. Sodium and water restriction:
 - Sodium 88 mmol/day (no added salt), in severe case 40 mmol/day.
 - Water 0.5–1 L/day (fluid restriction is not necessary, unless sodium is <125 mmol/L).
 - Avoid salt-containing and salt-retaining diets and drugs (NSAIDs, steroid and antacid).

3. Monitor weight, abdominal girth and urinary output daily. Weight loss should be 0.5–1 kg/day (fluid loss should not be more than 1 L daily).
4. Measure serum electrolyte and creatinine.
5. Few patients will respond to the above therapy.
6. If no response in 4 days with above therapy: Diuretic should be given. Aldosterone antagonist such as spironolactone 100–400 mg/day is given. If no response, either frusemide 40 mg daily is added. If no response with spironolactone 400 mg plus frusemide 160 mg daily, it is considered as refractory ascites. Prolonged use of spironolactone can cause painful gynaecomastia and hyperkalaemia. Eplerenone 25 mg once daily may be a suitable alternative (does not cause gynaecomastia).
7. If no response or refractory ascites:
 - Ensure that patient is not taking any salt or salt-containing diet or drugs.
 - If serum protein (mainly albumin) is low, diuretics may not respond. Then IV salt-poor albumin followed by IV frusemide may be given. Occasionally IV dextran may be tried.
8. Paracentesis:
 - It is indicated if there is huge ascites with cardiorespiratory embarrassment or resistant ascites.
 - 3–5 L of fluid can be removed. It is safe provided circulation is maintained (no fear of hepatic encephalopathy, thought previously). Paracentesis is followed by IV albumin (6–8 gm/L of ascetic fluid removed; usually 100 ml of 20% human albumin solution for every 3 L of ascitic fluid drained). Another plasma expander such as dextran (8 g/L of ascetic fluid removed) or haemaccel (125 mL/L of ascitic fluid removed) may be used.
9. Other modes of treatment (in resistant ascites):
 - LeVeen shunt (peritoneovenous): A catheter is used with one-way valve to communicate between peritoneal cavity and internal jugular vein, which allows ascitic fluid to pass directly into the systemic circulation (rarely done now-a-days). Its main complications are infection, SVC thrombosis, pulmonary oedema, bleeding from oesophageal varices and DIC.
 - TIPSS (transjugular intrahepatic portosystemic stent shunt): A stent is placed between portal vein and hepatic vein in liver to make portosystemic shunt, which is carried out under radiological control via internal jugular vein. It is mainly used to reduce portal pressure and also variceal bleeding. It can relieve resistant ascites but does not prolong life. Following its use, frequency of paracentesis and diuretic dose is reduced. It can be done provided reasonable liver function without encephalopathy and minimal disturbance of renal function (TIPSS is ineffective with intrinsic renal disease). Hepatic encephalopathy may occur following TIPSS. This can be managed by reducing the shunt diameter.
 - Portosystemic shunt surgery: Portocaval or splenorenal shunt. Rarely done now-a-days. May cause encephalopathy.
10. Liver transplantation may be considered, if all measures fail.

Q: Will you **prefer** paracentesis or TIPSS in refractory ascites?

A: TIPSS is preferable than repeated paracentesis, as large volume of fluid and protein are lost in paracentesis. Moreover, TIPSS can improve survival also.

Q: If patient of CLD with ascites complains of fever and abdominal pain, what is the likely **diagnosis?**

A: Spontaneous bacterial peritonitis (SBP) (other causes of fever in CLD with ascites are secondary infection, hepatoma and excess pyrogen accumulation).

Q: What are the **complications** of ascites in CLD?

A: SBP and hepatorenal syndrome.

Q: If patient with CLD **deteriorates**, what are the possibilities?

A: As follows:
- Spontaneous bacterial peritonitis.
- Hepatocellular carcinoma.

Q: What are the **bad prognostic signs** of CLD?

A: As follows:
1. Clinical:
 - Increasing jaundice.
 - Ascites.
 - Portosystemic encephalopathy.
2. Laboratory:
 - Increasing bilirubin.
 - Sodium <120 mmol/L (not due to diuretic).
 - Falling plasma albumin <30 g/L.
 - Prothrombin time: Prolonged.

Q: What **investigations** should be done in this case?

A: As follows:
1. LFT (total protein and A:G ratio, and prothrombin time are the two **most** important tests for CLD. Others are serum bilirubin, SGPT and alkaline phosphatase).

2. USG of whole abdomen (in cirrhosis, liver may be small, shrunken, coarse and of high echogenic texture, with splenomegaly, ascites and dilated portal vein).
3. Viral markers for HBV (HBsAg, HBeAg, anti-HBc) and for HCV (anti-HCV).
4. Proctoscopy (to test for haemorrhoid).
5. Endoscopy (to test for oesophageal varices).
6. CT scan of hepatobiliary system may be performed.
7. Liver biopsy under USG control (confirmatory).
8. If CLD is due to other cause investigation should be done accordingly, such as:
 - If haemochromatosis is suspected: Serum iron, TIBC and ferritin.
 - If PBC is suspected: Antimitochondrial antibody and other autoantibodies.
 - In younger age, if Wilson disease is suspected: Serum copper, ceruloplasmin and urinary copper.
 - If α_1-antitrypsin deficiency: Serum α_1-antitrypsin (which is sometimes associated with liver disease and also pulmonary emphysema, particularly in smokers).
9. Test for ascitic fluid (cytology, biochemistry, SAAG).
10. Other routine investigations:
 - CBC, ESR.
 - Serum urea and creatinine, electrolytes, blood sugar.

Q: What investigations are done to see the severity of liver disease?

A: As follows:

- Serum albumin: If <28 gm/L, outlook is poor.
- Prothrombin time: Prolong PT indicates severe liver disease.
- Serum electrolytes: Low sodium indicates severe liver disease due to a defect in free water clearance.
- Serum creatinine: High creatinine >130 µmol/L is a marker of worse prognosis.

Q: What is spontaneous bacterial peritonitis (SBP)?

A: It means infection of ascitic fluid in a patient with cirrhosis of liver in the absence of any apparently primary source of infection. SBP may develop in 8% cases (may be as high as 20–30%). It is usually by single organism (monomicrobial). Source of infection cannot be determined usually (so it is named as spontaneous). It is suspected in any patient with ascites who clinically deteriorates.

Causes of SBP: The infective organism gain access to the peritoneum by haematogenous route or mesenteric lymphatics. Most organisms are of enteric origin, mainly *Escherichia coli, Klebsiella, Haemophilus, Enterococcus,* other enteric Gram-negative organisms, rarely pneumococcus and streptococcus. Anaerobic bacteria are not usually associated with SBP.

Clinical features: In a patient with cirrhosis and ascites, may present with sudden abdominal pain, rebound tenderness, absent bowel sounds and fever. There may be increasing ascites, not responding to diuretic. Abdominal signs may be mild or absent in one-third patients. In these patients, hepatic encephalopathy and fever are the main features.

Ascitic fluid in SBP shows the following:

- Fluid looks cloudy (exudative is with high protein and low sugar).
- Neutrophil counts of fluid >250/mm^3.
- Ascetic culture in blood culture bottles gives the highest yield of organisms. C/S may be negative.

Treatment of SBP: Pending the result of culture, if neutrophil in ascitic fluid is high, treatment should be started immediately as follows:

- Broad-spectrum antibiotics: Cefotaxime 2 g 8–12 hourly for at least 5 days.
- Ceftriaxone **plus** amoxiclav is an alternative.
- Intravenous albumin may reduce mortality.

Prognosis and prevention of SBP: Mortality is 10–15%. SBP is an indication for referral to liver transplantation centre. Recurrence is common in 70% case within 1 year. This can be prevented by norfloxacin 400 mg daily or ciprofloxacin 500 mg once or twice daily or cotrimoxazole (1 double-strength tablet, 5 days/week). In any patient with acute variceal bleeding, risk of bacterial peritonitis may be reduced by giving injection ceftriaxone 1 g daily or oral norfloxacin. Also, patient with high-risk group in cirrhosis (low albumin, increased PT, low ascitic fluid albumin), norfloxacin may be used to prevent bacterial peritonitis.

N.B. Occasionally, there may be secondary bacterial infection other than SBP. To differentiate from SBP, the following features in ascitic fluid may suggest secondary bacterial infection:

- Neutrophil >10,000 (very high).
- Total protein: Very high (>1 g/dL is against SBP, highly suggestive of secondary bacterial infection).
- Glucose <50 mg%.
- Ascitic LDH > serum LDH.
- Presence of multiple organisms in culture.

Q: What is hepatorenal syndrome?

A: If a patient with cirrhosis and ascites develops renal failure, it is called hepatorenal syndrome. It occurs in 10% cases and is of two **types:**

- Type 1 hepatorenal syndrome is characterized by progressive oliguria and rapid rise in serum creatinine. There is no proteinuria; urine sodium excretion is low; <10 mmol/day and urine/plasma osmolality ratio is >1.5. Prognosis is poor; without treatment median survival is <1 month.
- Type 2 hepatorenal syndrome occurs with refractory ascites, characterized by moderate and stable increase of serum creatinine. Prognosis is better.

Mechanism of hepatorenal syndrome: Initially there is vasodilatation possibly due to nitric oxide, leading to hypotension. As a result, there is high plasma renin, aldosterone, norepinephrine and vasopressin, leading to vasoconstriction of the renal vasculature, causing increased preglomerular vascular resistance. There is reduced glomerular filteration rate (GFR), and also sodium and water retention.

Other mediators like eicosanoids may also be involved.

Renal failure is functional and tubular function is intact. Hepatorenal syndrome may be precipitated by excess diuretic therapy, NSAIDs, diarrhoea or paracentesis, and infection, especially spontaneous bacterial peritonitis.

Treatment:

- Diuretic should be stopped.
- Hypovolaemia should be corrected, preferably with albumin.
- Terlipressin or noradrenalin with intravenous albumin may be used.
- Liver transplantation is the best option.

Q: What is hepatopulmonary syndrome?

A: Hepatopulmonary syndrome is defined as hypoxaemia occurring in patient with advanced liver disease. PaO_2 is <9.3 kPa or 70 mmHg. It is due to intrapulmonary vascular dilatation with no evidence of primary pulmonary disease. Hypoxia is due to intrapulmonary AV communication.

The patient has features of cirrhosis with clubbing, spider angioma and cyanosis. Most patients have no respiratory symptoms. But with more severe disease, the patient is dyspnoeic on standing. There is a characteristic reduction of arterial oxygen saturation on standing.

Transthoracic echo shows intrapulmonary shunting (which is probably due to nitric oxide overproduction); and arterial gas analysis shows low oxygen saturation. HRCT may be helpful for detecting dilated pulmonary vessels.

Liver transplantation is indicated in hepatopulmonary syndrome. Features improve after liver transplantation.

Q: What is portopulmonary hypertension?

A: It is defined as pulmonary hypertension and cirrhosis of the liver with portal hypertension. There is normal pulmonary artery wedge pressure. It occurs in 1–2% cases of cirrhosis. It is caused by vasoconstriction and obliteration of the pulmonary arterial system due to circulating vasoconstrictors particularly endothelin 1. This leads to breathlessness and fatigue. It may respond to medical therapy.

Severe pulmonary hypertension is a contraindication for liver transplantation.

Read the Following Topics in Relation to CLD

Portosystemic Anastomosis

(Between portal and systemic veins)

Sites are:

1. At the lower end of oesophagus, oesophageal tributaries of left gastric vein (portal) communicate with oesophageal tributaries of hemiazygos veins (systemic).
2. At the lower end of rectum and anal canal, superior rectal vein (portal) communicates with middle and inferior rectal veins (systemic).
3. Anterior abdominal wall (around the umbilicus):
 - The paraumbilical vein (portal) communicates with systemic veins in epigastric, lateral thoracic, intercostal and lumbar veins.
 - Paraumbilical vein (portal) communicates with diaphragmatic veins (systemic) by a number of small veins, called accessory portal system of Sappey.
4. At bare area of liver, portal radicles of liver communicates with diaphragmatic veins (systemic).
5. At retroperitoneal site, the splenic and colic veins (portal) communicate with left renal veins and other tributaries of inferior vena cava (IVC) by small veins called veins of Retzius.
6. At the fissure for ligamentum venosum, rarely, persistent ductus venosus establishes direct portacaval anastomosis (in foetal life, left branch of portal vein at the porta hepatis communicates with IVC via ductus venosus. After birth, ductus venosus is fibrosed to form ligamentum venosum).

Spider Angioma

It consists of central arteriole from which numerous capillaries radiate, looks like spider legs. Size varies from pinhead to 1–2 mm (sometimes 1–2 cm). These are found along the area of superior vena cava (SVC), commonly in neck, face, chest and dorsum of hand, and above the nipple lines, cause of which is not known. Blanches on pressure, may pulsate if large. Better seen with glass slide or pinhead.



Spider angioma

Causes of spider angioma:

1. Physiological:
 - Rarely present in normal people (2%), 1–2 in number, common in children. If >2 in number, it is usually pathological, especially in male than female.
 - Pregnancy (usually in the third trimester, disappears after 2 months of delivery).
2. Pathological:
 - CLD is commonly alcoholic cirrhosis (disappears with improvement of liver function; appearance of new spider indicates deterioration of liver function).
 - Viral hepatitis (transient).
 - Oestrogen therapy and oestrogen-containing oral contraceptive pill.
 - Rarely, in rheumatoid arthritis, thyrotoxicosis.

Mechanism of spider angioma:

- Due to hyperdynamic circulation.
- Excess oestrogen level (due to reduced metabolism by the liver).

Differential diagnoses of spider angioma:

- Purpura (spontaneous bleeding into skin and mucous membrane, does not blanch on pressure and there is progressive colour change).
- Hereditary haemorrhagic telangiectasia.
- Campbell de Morgan spots.
- Venous stars.

Venous Stars

These are 2–3-cm lesions that occur on dorsum of foot, leg, back and lower chest. Caused by elevated venous pressure and are usually found overlying the main tributary of large veins. Do not blanch on pressure and blood flow is from periphery to the centre of lesion (opposite to spider angioma).

Palmar Erythema (Liver Palm)

Redness in thenar and hypothenar eminence, and pulp of fingers. Blanches on pressure. With glass slide, flushes synchronously with pulse.



Palmar erythema

Causes of palmar erythema:

1. Physiological:
 - Normal people; may be familial.
 - Pregnancy.
2. Pathological:
 - CLD (commonly alcoholic).
 - Thyrotoxicosis.
 - Polycythaemia.
 - Prolonged rheumatoid arthritis.
 - Chronic leukaemia.
 - Febrile illness.

Mechanism of palmar erythema in CLD:

- Hyperdynamic circulation.
- Probably, high oestrogen (controversial).

Q: Why itching in liver disease?

A: Common in primary biliary cirrhosis and obstructive jaundice. Actual cause is unknown, probably due to upregulation of opioid receptors and increased levels of endogenous opioids.

Q: What are the **vitamin K-dependent** coagulation factors?

A: Factors II, VII, IX and X (which are produced by liver).

Q: In which liver disease, vitamin K therapy is helpful?

A: Usually in obstructive jaundice, as bile salt is necessary for absorption of vitamin K. Less or not helpful in parenchymal liver disease, as vitamin K is not used or less used by the diseased liver.

N.B. PT depends on factors I, II, V, VII and X. In CLD, the PT is prolonged when these factors fall below 30%.

Flapping Tremor (Asterixis)

It is characterized by irregular, flexion–extension movement of wrist and metacarpophalangeal (MCP) joints, abduction–adduction of fingers, produced by dorsiflexion of wrist and spreading of the fingers. It is called flapping because of resemblance to a bird flapping its wings. It is demonstrated by asking the patient to stretch out arms in front, separate the fingers, dorsiflexion of wrist with fixed forearm by the examiner's hand.

If it is present, there is:

- Jerky, irregular, flexion–extension of wrist, and MCP joint **(looks like goodbye).**
- Accompanied by lateral movement of fingers or abduction–adduction of fingers.

Features of flapping tremor:

- It is absent at rest, produced by intentional movement, maximum at sustained posture.
- Usually bilateral, and not necessarily synchronous on each side.
- Disappears during coma.
- Occasionally arms, face, neck, tongue, jaw and lids are involved.

Causes of flapping tremor:

- Hepatic encephalopathy (the commonest cause).
- Severe cardiac failure.
- Respiratory failure.
- Renal failure.
- Others causes (rare): Cerebrovascular accident (CVA), drug toxicity (phenytoin and barbiturate), acute focal parietal or thalamic lesion (vascular), and hypoglycaemia.

Mechanism of flapping tremor in CLD:

- It is due to impaired inflow of joint position sense and other afferent informations to the brainstem reticular formation, resulting in rhythmical lapse of postural muscle tone.

Q: What is fetor hepaticus?

A: It is a bad smell (slightly faecal) of breath, like that of dead mouse, due to methyl mercaptan, exhaled in breath, derived from amino acid methionine, which is not deaminated by the diseased liver. Methyl mercaptan is of intestinal origin (reduced by defaecation or use of antibiotics). Presence of fetor hepaticus indicates severe hepatocellular failure with collateral circulation.

Q: What are the causes of bad breath (halitosis)?

A: As follows:

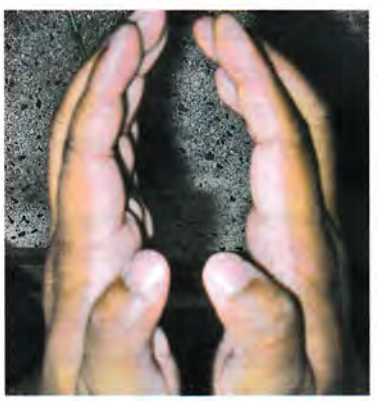
- Hepatic precoma (fetor hepaticus-like dead mouse).
- Diabetic ketoacidosis (sweetish due to ketone body).
- Uraemia (fishy ammoniacal).
- Lung abscess with anaerobic infection (may be foetid).
- Others are faulty oral hygiene and alcoholism.

Dupuytren Contracture

It is characterized by thickening, fibrosis and shortening of superficial palmar fascia, causing flexion contracture of fingers. The ring and little fingers are commonly affected and also other fingers are affected. Inability to extend the fingers fully is associated with puckering of the skin and presence of palpable nodules. Usually painless, bilateral, age related, five times common in male than in female, often familial with dominant inheritance. It may affect the sole of foot also. It is slowly progressive and fasciotomy is seldom necessary.



Dupuytren contracture



Diabetic cheiroarthropathy

Causes are:

- Cirrhosis of liver (commonly alcoholic).
- Alcoholism (itself, not by cirrhosis).
- Prolonged antiepileptic drug (phenytoin).
- Manual worker (gardener) and chronic vibration injury.
- Traumatic.
- Familial (as autosomal dominant, associated with Garrod patch on dorsum of hand).
- Diabetes mellitus (diabetic cheiroarthropathy, confused with systemic sclerosis).
- Peyronie disease.
- Idiopathic (in many cases).

N.B. It is confused with diabetic cheiroarthropathy.

Portosystemic Encephalopathy (PSE or Hepatic Precoma)

Definition: Portosystemic encephalopathy is a state of neuropsychiatric syndrome due to biochemical disturbance of brain function caused by CLD. It may progress from confusion to coma. Liver failure and portosystemic shunting are two important factors for PSE. It is reversible, does not cause marked pathological change in brain and may have cerebral oedema in advanced stage.

Mechanism of PSE: It is due to the nitrogenous substances of gut origin that enters into the brain. Normally, these substances are metabolized by healthy liver. In diseased liver, these are not metabolized and enters into the brain through portosystemic shunt.

PSE can occur in portal hypertension with cirrhosis, also after surgery like portocaval or TIPS shunt.

Nitrogenous substances are:

- Ammonia (produced by intestinal bacteria breaking down protein).
- γ-aminobutyric acid (GABA).
- Amino acid, mercaptan, fatty acids and octopamine, which act as false neurotransmitters.

Factors precipitating PSE (by increasing the availability of nitrogenous substance):

- High dietary protein.
- Gastrointestinal bleeding.
- Constipation.
- Drugs (sedative, antidepressants and diuretics).
- Infection including spontaneous bacterial peritonitis.
- Fluid and electrolyte imbalance (hypokalaemia).
- Trauma.
- Surgery (shunt surgery, TIPSS or other surgery).
- Paracentesis (> 3–5 L).
- Development of hepatocellular carcinoma.

Clinical features of PSE (remember the mnemonic **DPISTF**):

- **D: Disturbance** of consciousness (confusion, disorientation, drowsiness, delirium, stupor and later coma).
- **Disorder** of sleep (hypersomnia, inversion of sleep and more sleep in daytime).
- **P: Personality** change (childish behaviour, abnormal behaviour, apathy, irritability).
- **I: Intellectual** deterioration, from simple mathematical calculation to organic mental function. Earliest is constructional apraxia (see below).
- **S: Speech** disturbance (slow, slurred, monotonous and dysphasia) and **sleep** inversion (daytime sleeping).
- **T: Tremor** (flapping tremor).
- **F: Foetor** hepaticus (sweet musty odour in breath).

Other features are convulsion, exaggerated reflex, extensor plantar response and clonus. Rarely, chronic hepatic encephalopathy may be associated with cerebellar dysfunction, Parkinsonism, spastic paraplegia and dementia.

Q: What are the **differential diagnoses** of PSE?

A: As follows:

- Intracranial bleeding (subdural, extradural haematoma).
- Drug or alcohol intoxication.
- Delirium tremens (alcohol withdrawal).
- Hypoglycaemia.
- Wernicke encephalopathy.
- Primary psychiatric disorder.
- Neurological Wilson disease.
- Postictal state.

Q: How to **diagnose** PSE in early stage?

A: By EEG, which shows diffuse slowing in frequency of normal α-range (8–13 Hz) to δ-range (1.5–3 Hz). However, diagnosis is mostly clinical.

Q: How to **treat** PSE?

A: As follows:

- Possible precipitating factors should be identified and avoided (drugs, constipation, electrolyte imbalance, bleeding).
- **No** sedative and **no** diuretic. No protein restriction is recommended.
- Nutrition: Glucose (300–400 g/day) orally. If the patient cannot take by mouth, then IV should be given.

- Lactulose: 15–30 mL 8 hourly (bowel should move at least twice daily). If the patient is unable to take lactulose by mouth, it can be given per rectally (300 mg lactulose in 700 ml saline or sorbitol as retention enema). Lactitol is an alternative to lactulose.
- Low bowel wash (if no response to lactulose, then enema).
- Gut sterilizer: Metronidazole (200 mg 8 hourly) or neomycin 1–4 g, 4–6 hourly (it is ototoxic, less or not used). Rifaximin 400 mg three times daily orally is more preferable (not absorbed).
- Correction of electrolyte imbalance (especially hypokalaemia).
- Control of infection by antibiotic.
- It is suggested that eradication of *Helicobacter pylori*, which is ammonia-producing may help (not proved).
- Chronic or refractory hepatic encephalopathy is an indication for liver transplantation.
- Other treatment: Zinc deficiency should be corrected, if present.
- If the patient is agitated: Oxazepam (10–30 mg) may be given by mouth.
- Other therapy includes flumazenil—a benzodiazepine receptor antagonist (may help in some cases).

Q: What is the **mode of action** of lactulose?

A: Lactulose is a nonabsorbable disaccharide, reaches the colon intact and is metabolized by colonic bacteria to lactic acid. It acts in the following way:

- Osmotic laxative.
- Lactic acid reduces pH of colonic contents, inhibits ammonia-producing colonic bacteria and reduces ammonia absorption by converting NH3–NH4, which is not absorbed.
- Promotes incorporation of nitrogen into bacteria.

Q: What is **fulminating hepatic failure**?

A: It is a clinical syndrome of encephalopathy characterized by confusion, stupor and coma, resulting from sudden severe impairment of hepatic function, occurring within 8 weeks of onset in the absence of pre-existing liver disease. It is also called acute liver failure. It may be hyperacute (<7 days), acute (within 8–28 days) or subacute (29 days to 12 weeks) between the onset of jaundice and encephalopathy.

The two **commonest causes** are viral hepatitis (commonly B and E, and rarely A) and paracetamol toxicity. Other causes are acute fatty liver in pregnancy, Wilson disease, following shock and rarely extensive malignancy of liver.

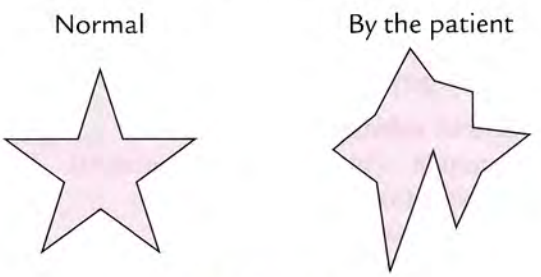
Clinical features are similar to PSE.

Treatment is also similar to PSE. Liver transplantation may be considered.

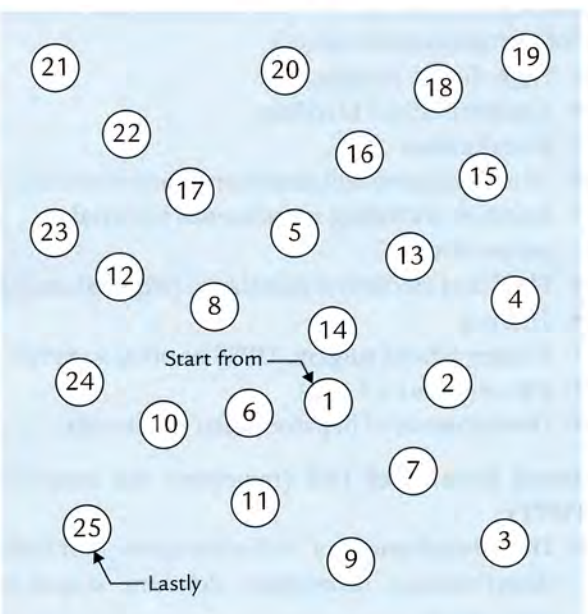
Q: What is **constructional apraxia**? How to test for it?

A: Constructional apraxia means inability to perform a known act in the absence of any motor or sensory disturbance. It is tested in the following way (patient will be unable to do):

- Ask the patient to draw a star.
- Writing disturbance (unable to write or disturbance in writing).
- Ask the patient to make triangle with three match sticks or ask to lighten the cigarette by match stick.
- Reitan trail making test (it is the ability to join or connect the numbers with a pen in a certain fixed time). It becomes prolonged in PSE.



Drawing star



From 1 to 25 numbered circles can be joined within 30 second normally; more time is required in PSE

Hepatomegaly (Primary Biliary Cirrhosis)

Presentation of a Case

- The abdomen is distended, flanks are full and skin is hyperpigmented.
- Umbilicus is everted.
- Superficial veins are visible with normal flow (away from umbilicus).
- Liver is palpable, ... cm from right costal margin in the midclavicular line, nontender, firm in consistency, with smooth surface and sharp margin. There is no hepatic bruit.
- Spleen is palpable, ... cm from the costal margin in left anterior axillary line, towards the right iliac fossa.
- Fluid thrill and shifting dullness: Present.

My diagnosis is hepatosplenomegaly with ascites.

Q: What is the **likely cause**?
A: CLD with portal hypertension.

Q: What **else** do you like to see?
A: Stigmata of CLD.

Q: In this middle-aged lady, what may be the **cause**?
A: May be due to HBV or HCV, or primary biliary cirrhosis.

Q: If it is PBC, what **else** do you like to see?
A: As follows:

- Jaundice.
- Xanthelasma.
- Xanthomatous deposit (in elbow, knee, buttock, hand crease and tendo calcaneus).
- Pigmentation (may be generalized).
- Scratch mark of itching.



Xanthelasma in PBC



Xanthoma in elbow



Xanthoma in palm



Xanthoma in buttock



Xanthoma in tendo calcaneus

Q: What are the **diseases associated** with PBC?

A: PBC is an autoimmune disease; it may be associated with other autoimmune diseases such as:

- Sjogren syndrome.
- Thyroid disease (hypothyroidism should be considered, especially with fatigue).
- Systemic sclerosis.
- Rheumatoid arthritis.
- Renal tubular acidosis.
- Dermatomyositis.
- Addison disease.
- Membranous glomerulonephritis.
- Fibrosing alveolitis.

N.B. There is high incidence of coeliac disease in PBC. It should be excluded when a patient presents with features of malabsorption.

Q: How the patient with PBC usually presents?

A: Common in females, middle-aged, of 40–60 years of age:

- Asymptomatic, isolated hepatomegaly on routine examination. High alkaline phosphatase in LFT.
- Pruritus may be the early feature; it may precede jaundice by many months.
- Jaundice (usually with pruritus).
- Abdominal pain or discomfort.
- Features of malabsorption.
- Fever, malaise, weakness, loss of weight.
- Others are hepatic osteodystrophy (characterized by bony pain or fracture due to osteomalacia or osteoporosis from malabsorption).

Q: What is **primary biliary cirrhosis**? What are the **causes**?

A: PBC is a chronic, progressive, cholestatic liver disease characterized by granulomatous destruction of interlobular bile ducts, inflammatory damage with fibrosis spreading from portal tract to liver parenchyma and eventual cirrhosis.

Causes: Actual cause is unknown. It is probably an autoimmune disease occurring in a genetically predisposed person, triggered by environmental factors like infections by retrovirus, bacteria including *E. coli* and mycobacteria. None are proved.

Q: What is **secondary biliary cirrhosis**?

A: When cirrhosis develops due to prolonged obstruction of the large biliary ducts. Causes are stone, strictures and sclerosing cholangitis.

Q: **Why itching** in PBC?

A: Actual cause of itching is unknown; but probably it is due to upregulation of opioid receptors and increased level of endogenous opioids. This is why opioid antagonist (naltrexone) is used to control itching in PBC.

Q: What **investigations** are done in PBC?

A: As follows:

- LFT (alkaline phosphatase is very high; may be the only finding. Aminotransferases may be elevated, but not more than five times of the upper limit. γ-glutamyl transpeptidase (γ-GT) is also high. Serum total protein and albumin is reduced. There is marked rise of 5-nucleotidases activity).
- USG (hepatomegaly with cirrhotic change, splenomegaly and ascites).
- Antimitochondrial antibody is positive in 95% cases (M2 is specific). Other antibodies such as antismooth muscle antibody (35%) and antinuclear antibody (25%) may be present.
- Liver biopsy (There is infiltration of lymphocytes and plasma cells in portal tract, destruction of small bile duct with ductal proliferation, piecemeal necrosis and cirrhosis. Granuloma may be present in 40% cases).
- Endoscopic retrograde cholangiopancreatography (ERCP) or magnetic resonance cholangiopancreatography (MRCP) (to rule out extrahepatic biliary obstruction in doubtful cases).
- Others: Serum cholesterol (high) and serum immunoglobulin (IgM) is very high.

Q: What is **antimitochondrial antibody (AMA)**?

A: It is an antibody directed against mitochondrial pyruvate dehydrogenase complex (PDC) of mitochondrial enzymes. There are four types of antigens (M2, M4, M8 and M9) of which M2 is specific for PBC. Five M2-specific antigens have been further identified, of which E2 component of the PDC is the major M2 autoantigen.

AMA is present in 95% cases of PBC, detected by ELISA (>1:160). It may be positive in autoimmune hepatitis (20%). It is not related to severity and prognosis.

Q: What are the **causes of granuloma in liver**?

A: As follows:

- PBC.
- Tuberculosis.
- Sarcoidosis.
- Brucellosis.
- Parasitic (strongyloidiasis).
- Schistosomiasis.
- Drug (phenylbutazone).

Q: What is the **best indicator for prognosis**?

A: Serum bilirubin (if >100 mmol/mL, liver transplantation should be considered).

Q: How to treat this patient?

A: As follows:

- Ursodeoxycholic acid 10–15 mg/kg (It improves bile flow, replaces toxic hydrophobic bile acid in the bile acid pool, reduces apoptosis of the biliary epithelium. It also improves LFT, slows down histological progress).
- For pruritus, cholestyramine is given, 4–16 g/day orally, usually with orange juice. Main dose (8 g) is given before and after breakfast (as duodenal bile acid secretion is more). Alternatively, rifampicin 300 mg/day or naltrexone (opioid antagonist) 25 mg/day up to 300 mg/day may be given. Naloxone is an alternative. In intractable itching, plasmapheresis or liver-support device [(molecular absorbent recirculating system (MARS)] may be considered. Liver transplantation may be indicated in intractable pruritus.
- Vitamins A, D, K and calcium supplement, alfacalcidol (1 mg/day orally).
- If osteoporosis: Bisphosphonate (such as risedronate may be used).
- Liver transplantation should be considered in liver failure. 5-year survival is over 80%, but recurrence of PBC after transplantation occurs in one-third of cases at 10 years.

N.B. Remember the following points:

- Colchicine 0.6 mg orally twice daily and methotrexate 15 mg/weekly may be helpful in improving symptoms in some cases.
- Steroid improves biochemical and histological disease, but aggravates osteoporosis and other side effects, and should not be used.
- Azathioprine, penicillamine and cyclosporine have no beneficial role.
- In asymptomatic patient, follow-up should be done.

Q: What are the **indications of liver transplantation** in PBC?

A: As follows:

- Advanced liver disease (increasing jaundice with serum bilirubin >100 µmol/L).
- Intractable pruritus.

Q: How **cholestyramine** works?

A: It is a chelating agent, acts by binding pruritogens in intestine and increases excretion in stool. It is ineffective in complete biliary obstruction.

Q: What is the **prognosis** of PBC?

A: As follows:

- Asymptomatic patients or patients presenting with pruritus: Survive for more than 20 years.
- Once symptoms like jaundice develop, average survival is around 5 years (may be 7–10 years).

Q: What is the risk of **hepatobiliary malignancy** in PBC?

A: It is increased in PBC. Risk factors for malignancy are older age, male sex, prior blood transfusion, and signs of cirrhosis and portal hypertension.

Hepatomegaly (Haemochromatosis)

Presentation of a Case

- The abdomen is distended; flanks are full with everted umbilicus.
- Skin is hyperpigmented.
- Liver is palpable, ... cm from right costal margin in the midclavicular line, nontender, firm in consistency, with smooth surface and sharp margin. There is no hepatic bruit.
- Spleen is palpable, ... cm from the costal margin in left anterior axillary line, towards the right iliac fossa.
- Fluid thrill and shifting dullness: Present.

My diagnosis is hepatosplenomegaly with ascites.

Q: What is the **likely cause**?

A: CLD with portal hypertension.

Q: What **else** do you like to see?

A: Stigmata of CLD. Also, pigmentation in other parts of the body and arthritis.

Q: If **pigmentation and arthritis** are present what is the likely diagnosis?

A: Haemochromatosis.

Q: What are your **differential diagnoses**?

A: As follows:

- Decompensated cirrhosis of liver due to HVB or HCV infection or metabolic cause.
- Primary biliary cirrhosis.

Q: If PBC, what are the findings?

A: PBC is more common in middle- aged female, with longstanding generalized itching. Also, there may be xanthelasma, xanthoma, etc.

Q: What is the **size of liver** in cirrhosis?

A: Small.

Q: Can the liver be enlarged in cirrhosis?

A: Liver may be enlarged if cirrhosis is due to haemochromatosis, primary biliary cirrhosis and alcoholic cirrhosis (early stage).

Q: What investigations should be done in haemochromatosis?

A: As follows:

1. CBC.
2. Liver function tests.
3. Iron profile:
 - Serum iron (increased).
 - Total iron-binding capacity (>70% is saturated).
 - Serum ferritin (increased, >600 µg/L).
4. CT scan or MRI of hepatobiliary system (increased density of liver due to iron deposits). MRI has high specificity for iron overload, but less sensitivity.
5. Hepatic iron index (HII): Shows quantification of liver iron, HII >1.9 suggests genetic haemochromatosis.
6. Liver biopsy (iron deposition, hepatic fibrosis, cirrhosis). Liver biopsy to measure the iron stores is a definitive test.
7. Others: Blood sugar, ECG, X-ray chest, echocardiogram, X-ray of the involved joint (shows chondrocalcinosis).

Q: What are the causes of haemochromatosis?

A: As follows:

1. Primary: Hereditary disorder, inherited as autosomal recessive.
2. Secondary:
 - Haemolytic anaemia:
 - β-Thalassaemia.
 - Sideroblastic anaemia.
 - Chronic haemolytic anaemias.
 - Exogenous iron overload:
 - Repeated blood transfusion (transfusion siderosis).
 - Repeated iron injection.
 - Prolonged oral iron.
 - Chronic liver diseases:
 - Hepatitis C.
 - Porphyria cutanea tarda.
 - Alcoholic cirrhosis (in advanced stage).

Q: What is primary haemochromatosis?

A: This is a hereditary disorder, inherited as autosomal recessive, characterized by excess deposition of iron in various organs, leading to fibrosis and functional organ failure. It is associated with HLA-B_3, B_7 and B_{14}. It is more in male, less in female; but in postmenopausal case, it is also more in female.

N.B. Normal body iron is 3–4 g. In haemochromatosis, it may be 20–60 g. Mainly iron is deposited in liver and pancreatic islets; also in endocrine glands (pituitary, adrenal), heart and skin.

Q: Why is haemochromatosis less in female?

A: Females are protected by iron loss in menstruation and pregnancy.

Q: What is the mechanism (pathogenesis) of primary haemochromatosis?

A: In haemochromatosis, mucosal absorption of iron is more and inappropriate to the body needs. Ultimately progressive accumulation of iron causes elevation of plasma iron, increase saturation of transferrin and high level of ferritin, which is deposited in different organs of the body.

Q: What are the common features of haemochromatosis?

A: Usually it occurs in male above 40 years. Common features are:

- Liver involvement: Hepatomegaly, CLD (about 30% may develop HCC).
- Skin pigmentation (leaden-grey skin pigmentation due to melanin deposition).
- Diabetes mellitus.
- Cardiac dysfunction (dilated cardiomyopathy, CCF, arrhythmia).
- Arthritis and chondrocalcinosis.
- Hypogonadism.

N.B. In a patient with CLD, if there are cardiac disease, arthritis, skin pigmentation and diabetes, haemochromatosis is very likely.

Q: What type of diabetes occurs in haemochromatosis?

A: This is called 'bronze diabetes' due to the bronze colouration of the skin.

Q: What are the common causes of pigmentation?

A: As follows:

- Addison disease.
- Haemochromatosis.
- Kala-azar.
- Arsenicosis.
- Drugs: Amiodarone, busulphan, bleomycin, phenothiazine, phenytoin, psoralen
- Systemic sclerosis.
- Alkaptonuria.
- Nelson syndrome.
- Chronic debilitating illness (malignancy, CLD, CRF).

Q: What are the causes of **raised ferritin level?**

A: As follows:

- Haemochromatosis.
- Alcoholic liver disease.
- Hepatitis C infection.
- Nonalcoholic steatohepatitis.
- As an acute phase reactant in inflammatory and neoplastic conditions.

Q: How do you **treat** haemochromatosis?

A: As follows:

- Weekly or twice weekly venesection of 500 ml blood (200–250 mg of iron) until the serum ferritin is normal. It may take 2 years of more. The aim is to reduce ferritin to <50 µg/L. Thereafter, venesection is continued as required to keep the serum ferritin normal (usually 3–4 venesections/year is needed). Following venesection, most of the symptoms improve or disappear, except testicular atrophy, diabetes mellitus and chondrocalcinosis. Joint pain may even worsen.
- Chelation therapy with desferrioxamine (40–80 mg/kg/day subcutaneously) may be given. It removes 10–20 mg of iron/day. It is mainly used if the patient cannot tolerate venesection, especially those with cardiac disease or severe anaemia.
- Symptomatic treatment of cirrhosis, diabetes mellitus (usually by insulin), CCF and cardiac arrhythmia.
- Alcohol must be avoided.
- Supplemental vitamin C must be avoided, as pharmacological doses can accelerate iron mobilization to a level that saturates circulating transferrin, resulting in an increase in pro-oxidant and free radical activity.
- First-degree family members should be screened.

N.B. In primary haemochromatosis, iron is deposited in hepatocytes; whereas in secondary iron overload, iron accumulates in Kupffer cells.

Q: What is the **cause of death** of haemochromatosis?

A: Death is usually due to cardiac failure (30%), hepatocellular failure or portal hypertension (25%), and HCC (30%).

Q: What is the **risk of HCC** in haemochromatosis?

A: HCC usually occurs as late sequelae in patient who is cirrhotic at presentation. It does not occur if the disease is treated in the precirrhotic stage. In presence of cirrhosis, venesection reduces but does not abolish the risk of HCC.

Q: What is the **prognosis**?

A: If it is diagnosed and treated in precirrhotic stage, life expectancy is normal. Even in cirrhotic patients, there is a good prognosis compared to other causes of cirrhosis. Three-fourth cases survive 5 years after the diagnosis.

Ascites

Presentation of a Case

- There is generalized distension of abdomen, flanks are full, umbilicus is everted.
- Shifting dullness is present.
- Fluid thrill is present (mention if any).

My diagnosis is **ascites.**

Q: What are the **causes** of abdominal distension?

A: Fluid, fat, flatus, faeces and foetus (five Fs). Others—intra-abdominal mass.

Q: **Why** ascites?

A: Shifting dullness (fluid thrill in tense ascites).



Ascites

Q: How to **confirm** ascites clinically?

A: By eliciting shifting dullness; also fluid thrill (which is present in tense ascites).

Q: What **relevants** do you like to see?

A: As follows:

- Stigmata of CLD (page 202).
- Generalized swelling in face, leg, other parts of the body (nephrotic syndrome, hypoproteinaemia).
- Neck vein, leg oedema and heart (CCF and chronic constrictive pericarditis).
- Lymph node (lymphoma and disseminated TB).

Q: What are the **causes** of ascites in this case?

A: Mention the causes of that patient in relation to age, also sex:

- Cirrhosis of liver with portal hypertension (the commonest cause, in 80% cases).
- Intra-abdominal malignancy with peritoneal metastasis.
- Infection (tuberculous or pyogenic peritonitis).
- CCF.
- Others: Hepatoma with secondary in the peritoneum, hypoproteinaemia due to any cause, Meigs syndrome (in female).

N.B. Common causes of ascites:

- Cirrhosis of liver with portal hypertension.
- Intra-abdominal malignancy with peritoneal metastasis (usually ovarian and GI).
- CCF.

Q: What is **ascites**? How much **fluid** is required to detect ascites?

A: It is the pathological accumulation of free fluid in peritoneal cavity. Usually 2 L fluid is necessary to detect clinically (at least 1 L is necessary, even in thin person). Pleural effusion may be present in 10% cases with ascites, usually on the right side, mostly small, occasionally massive and unusual on left side.

N.B. Normally, no or little fluid is present in peritoneal cavity. In a female, up to 20 mL may be present, varies with menstruation.

Q: If the patient has **cirrhosis** and **ascites**, what does it **indicate**?

A: Decompensated cirrhosis with portal hypertension (a bad prognostic sign).

Q: What is the **character** of ascitic fluid in CLD?

A: Usually clear; may be straw or light-green coloured and transudative.

Q: What is the **single best investigation** to detect ascites?

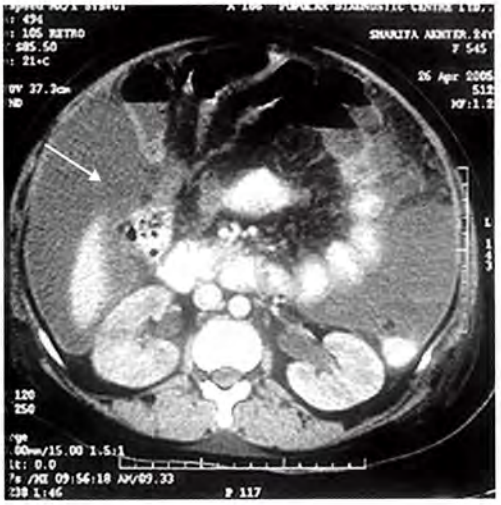
A: Ultrasonography.

Q: What **investigations** are done in ascites?

A: As follows (according to suspicion of cause):

1. If CLD is suspected, LFT should be done (see CLD).
2. CBC (high ESR in TB and leucocytosis in pyogenic infection).
3. Chest X-ray (TB, cardiomegaly and chronic constrictive pericarditis).
4. USG of abdomen (to see liver, paraaortic lymph nodes, neoplasm and ovary in female).
5. Ascitic fluid tap for the following tests:
 - Naked-eye examination (straw coloured, blood stained, serous and chylous).
 - Gram staining and C/S (in pyogenic infection).
 - Cytology (neutrophil >250 cells/mm^3 or WBC >500 cell/mm^3 in SBP, high lymphocyte in tuberculous peritonitis).
 - Biochemistry for protein and sugar shows high protein in exudative and low protein in transudative. Simultaneous serum albumin to see **serum ascitic albumin gradient** (see below).
 - If tuberculous peritonitis is found, fluid for ADA, AFB and mycobacterial C/S, PCR.
 - Exfoliative cytology (to see malignant cells).
6. Other tests (according to suspicion of causes):
 - For tuberculous peritonitis: MT.
 - Urine for proteinuria and serum total protein (nephrotic syndrome).
 - Ascitic fluid amylase in acute pancreatitis (>1000 is highly suggestive).
7. CT scan or MRI (if any growth or mass suspected).
8. Laparoscopy and biopsy.





Ascites

Serum-ascites albumin gradient (SAAG): It is the difference of albumin between serum and ascitic fluid (calculated by serum albumin minus ascitic albumin). This gradient correlates directly with portal pressure. It is the single test to differentiate ascites due to portal hypertension from nonportal hypertension.

- If the gradient is >1.1 g/dL, it indicates CLD with portal hypertension.
- If <1, no portal hypertension (Ascites due to nonportal hypertension will be noted. It is 97% accurate.)

N.B. Ascites protein <25 g/L and SAAG >1.1 g/dL is usually suggestive of portal hypertension.

Read the Following Points in Relation to Ascites

Causes of ascites:

1. Liver diseases (cirrhosis of liver with portal hypertension, hepatoma with secondary in peritoneum, Budd–Chiari syndrome).
2. Abdominal causes (intra-abdominal malignancy with peritoneal metastasis, such as carcinoma of kidney, stomach, colon and ovary).
3. Peritoneal causes are peritonitis (TB or pyogenic) and secondaries in the peritoneum.
4. Cardiovascular (chronic constrictive pericarditis and CCF).
5. Hypoproteinaemia (nephrotic syndrome, malnutrition and malabsorption).
6. Others:
 - Collagen disease (SLE and PAN).
 - Lymphoma and leukaemia.
 - Meigs syndrome (ovarian fibroma, ascites and right-sided pleural effusion).
 - Acute pancreatitis.
 - Myxoedema.
 - Chylous ascites.

Ascites may be exudative or transudative:

1. **Transudative causes** (protein <25 g/L):
 - Cirrhosis of liver with portal hypertension.
 - Nephrotic syndrome.
 - CCF.
 - Meigs syndrome.
 - Other causes of hypoproteinaemia (malnutrition and malabsorption).
2. **Exudative causes** (protein >25 g/L):
 - Peritonitis (TB and pyogenic).
 - Malignancy.
 - Collagen disease.
 - Myxoedema.
 - Budd–Chiari syndrome.
 - Others are acute pancreatitis and chylous ascites.

Causes of hepatomegaly with ascites:

- HCC due to cirrhosis of liver lesion.
- Hepatoma with secondary in the peritoneum.
- Congestive cardiac failure or chronic constrictive pericarditis.
- Lymphoma.
- Disseminated TB.
- Budd–Chiari syndrome.
- Decompensated cirrhosis of the liver due to metastatic cause.
- Alcoholic hepatitis
- Secondary in the liver with peritoneal carcinomatosis.

Causes of splenomegaly with ascites:

- Decompensated cirrhosis of liver with portal hypertension.
- Collagen disease (SLE).
- Lymphoma.
- Leukaemia.
- Disseminated TB.

Causes of haemorrhagic ascites:

- Traumatic.
- Malignancy.
- Ruptured ectopic pregnancy.
- Acute haemorrhagic pancreatitis.
- Rupture of spleen.
- Any cause of bleeding disorder.
- Excess anticoagulant.
- Occasionally, tuberculous peritonitis.

Causes of straw-coloured ascites:

- Tuberculous peritonitis.
- Occasionally, cirrhosis of liver.

Causes of cloudy ascites:

- Pyogenic infection.
- SBP.

Causes of chylous ascites (milky colour, high triglyceride and Sudan staining of ascitic fluid shows fat cells):

- Trauma.
- Filariasis.
- Tuberculosis.
- Malignancy.

Abdominal Mass

The mass or masses in abdomen described here exclude liver, spleen and kidney.

Once a mass is palpable in the abdomen, **ensure** whether it is intra-abdominal or extra-abdominal, while the patient is in supine position. For this, ask the patient to keep the arms across the upper chest and raise the head upward up to halfway (rising test). Or, ask the patient to raise both the extended legs from the bed (leg lifting test). Now look at the mass. The intra-abdominal mass will either disappear or decrease in size; and the extra-abdominal mass will be more prominent.

Once a mass is felt, the following points must be seen very carefully:

- Site.
- Size.
- Surface (regular or irregular).
- Consistency.
- Tenderness.
- Margin.
- Mobility (fixed or mobile).

Present the case systematically. Examiner may ask, **'What are the differential diagnoses?' 'How to investigate?'** One must mention the possible differential diagnosis according to the site of mass and age of the patient.

Presentation of a Mass in Anterior Abdominal Wall

- There is a mass in the right upper abdomen, 4 × 5 cm, surface is smooth, margin is slightly irregular, firm in consistency, nontender and fixed to the overlying skin.

My differential diagnoses are (mention according to your finding):

- Lipoma
- Fibroma
- Neurofibroma.

Other causes of mass in the anterior abdominal wall:

- Sebaceous cyst.
- Dermoid.
- Malignant deposit.
- Melanoma.
- Epigastric hernia.
- Umbilical or paraumbilical hernia).
- Incisional hernia.
- Rectus sheath divarication.
- Haematoma.
- Parietal abscess.

Causes of Mass in Different Sites of Abdomen

Presentation of a Mass in Epigastrium

- There is a mass in epigastric region (extending in right or left hypochondrium). It is 6 × 7 cm, smooth (or irregular), nontender (or tender), ill-defined margin (or round margin), firm (or hard) in consistency and not freely movable.

Q: What are the causes of epigastric mass?

A: As follows (mention according to the findings and also age of the patient):

If the patient is middle-aged or elderly, the causes are:

1. Mass in left lobe of liver (hepatoma, secondaries and hydatid cyst).
2. Carcinoma of stomach.
3. Lymphoma of stomach.
4. Carcinoma of head of the pancreas.
5. Others:
 - Due to tender mass (liver abscess).
 - May be soft and cystic mass (pancreatic pseudocyst).
 - Mass in transverse colon (carcinoma).

- Pulsating mass (aneurysm of abdominal aorta).
- Epigastric hernia.

If the patient is young, causes are:

1. Lymphoma of stomach.
2. Mass in left lobe of liver (hydatid cyst, hepatoma, if tender mass—may be liver abscess).
3. Epigastric hernia.
4. Pancreatic pseudocyst.

Q: What relevant do you like to see if there is epigastric mass?

A: As follows:

- Virchow gland (due to secondaries from stomach).
- Lymph nodes in other parts of the body (lymphoma).
- If hepatic mass is suspected: Look for jaundice, evidence of CLD, primary source (e.g. testicular mass).
- Jaundice, scratch mark, pigmentation, etc. (carcinoma head of the pancreas causing obstructive jaundice).

Q: Mention one investigation that will help the diagnosis.

A: USG.

Q: What investigations should be done?

A: As follows (mention according to the suspicion of causes):

1. USG (It will give clue about mass—hepatic, pancreatic, stomach or colon.)
2. Other investigations according to the findings in ultrasonography:
 - If gastric mass: Endoscopy and biopsy (carcinoma of stomach and lymphoma).
 - If hepatic mass: Investigate accordingly (hepatoma, secondaries and hydatid cyst).
 - If pancreatic mass: CT scan or MRI, ERCP.
 - If colonic mass: Barium enema, colonoscopy and biopsy.

Presentation of a Mass in Right Iliac Fossa

- There is a mass in right iliac fossa, 4 × 6 cm, smooth (or irregular), nontender (or tender), ill-defined margin (or round margin), firm (or hard) in consistency, and freely movable from underlying structure and overlying skin.

Q: What are the causes of mass in right iliac fossa?

A: Tell the causes according to the age of the patient:

If the patient is young or early-aged:

- Appendicular lump (tender).
- Ileocaecal TB.
- Crohn disease.
- Lymphoma.
- Amoeboma (less common nowadays because of wide use of metronidazole).
- Others are actinomycosis, *Yersinia* infection, tubo-ovarian mass in female, pelvic kidney, tumour in undescended testes, ectopic kidney.

If the patient is elderly or middle-aged:

- Appendicular lump (tender).
- Ileocaecal TB.
- Carcinoma of caecum (hard, irregular and nontender).
- Lymphoma.
- Others may be as above.

N.B. If there is scar mark in lumbar area, diagnosis is transplanted kidney.

Q: How to diagnose?

A: History of the patient, physical examination and investigation.

Q: Mention one investigation that will help the diagnosis.

A: USG.

Q: What investigations do you suggest?

A: According to suspicion of causes:

- Hb%, TC, DC and ESR (high in TB; leucocytosis in appendicular mass).
- USG of whole abdomen.
- If ileocaecal TB (chest X-ray, MT).
- CT or MRI.
- FNAC (CT-guided or USG-guided).
- Barium enema (double contrast).
- Barium meal and follow-through with spot film in ileocaecal region (TB and Crohn disease).
- Colonoscopy and biopsy.
- If still no diagnosis is possible, then laparoscopy and biopsy.
- Occasionally, laparotomy may be required.

Presentation of a Mass in Left Iliac Fossa

- There is a mass in left iliac fossa, 3 × 4 cm, smooth (or irregular), nontender (or tender), ill-defined margin (or round margin), soft in consistency, and freely movable from underlying structure and overlying skin.

Q: What are the causes of mass in left iliac fossa?

A: Causes are (mention according to the age of the patient):

If the patient is young (or also any age), the causes are:

- Thick colon (in irritable bowel syndrome).
- Faecal mass (mass indented and moulded by pressure).
- Occasionally, normal colon may be palpable.
- Carcinoma of colon (rare).
- Diverticulitis.
- Tubo-ovarian mass in female.
- Pelvic kidney.

If the patient is elderly, the causes are:

- Carcinoma of colon (descending or sigmoid colon).
- Diverticulitis (tender, mobile mass).
- Faecal mass.

N.B. If laparotomy scar is present, the diagnosis is transplanted kidney. Examine for AV fistula and anaemia.

Q: What investigations do you suggest?

A: As follows:

- USG of whole abdomen.
- Barium enema (double contrast).
- Sigmoidoscopy and biopsy (if needed).
- Stool for occult blood.
- FNAC (CT-guided or USG-guided).
- Laparoscopy.
- Occasionally, laparotomy may be needed.

Presentation of a Mass in Right Hypochondrium

- There is a mass in right hypochondrium, 5 × 6 cm, margin is smooth (or irregular), surface is irregular, nontender, soft in consistency and freely movable from underlying structure and overlying skin.

Q: What are the likely causes of mass in right hypochondrium?

A: As follows:

- Mass in liver (hepatoma, secondaries and hydatid cyst).
- Gall bladder mass (carcinoma, mucocoele or empyema of gall bladder).
- Mass in right side of colon (malignancy).
- Carcinoma head of pancreas.

Causes of palpable gall bladder without jaundice

- Mucocoele.
- Empyema.
- Occasionally, carcinoma of gall bladder.

Causes of palpable gall bladder with jaundice

- Carcinoma of head of pancreas.
- Carcinoma of ampulla of Vater.
- Stone in common bile duct.
- Pressure from outside on bile duct (lymphoma and secondaries).
- Cholangiocarcinoma.
- Sclerosing cholangitis.

Q: What investigations do you suggest?

A: As follows:

- USG of hepatobiliary system.
- LFT.
- CT or MRI.
- ERCP.
- Laparoscopy.

Q: Could it be gall stone with palpable gall bladder?

A: Unlikely (but gall bladder is palpable, if the stone is in common bile duct).

Q: What is Courvoisier's law?

A: It is as follows:

- In a jaundiced patient with palpable gall bladder, the cause is unlikely to be gall stones; rather it is due to carcinoma head of pancreas and extrinsic pressure in bile duct.

Reverse of the law is:

- Obstructive jaundice without palpable gall bladder is unlikely to be carcinoma head of pancreas and extrinsic pressure in common bile duct.

Q: Why gall bladder is not palpable in gall stone disease?

A: Gall stone is associated with chronic cholecystitis and gall bladder is fibrosed, which is unable to enlarge.

Presentation of a Mass in Left Hypochondrium

- There is a mass in left hypochondrium, 3 × 4 cm, smooth (or irregular), nontender (or tender), ill-defined margin (or round margin), soft in consistency, and freely movable from underlying structure and overlying skin.

Causes of mass in left hypochondrium:

- Splenomegaly.
- Enlarged left kidney.
- Carcinoma of the stomach.
- Carcinoma of the splenic flexure of colon.
- Carcinoma or any mass on tail of pancreas.
- Omental mass.

Q: What investigations do you suggest?

A: As follows:

- USG of hepatobiliary system: This will show whether it is spleen or other mass. Then other investigation should be done according to suspicion of cause.

Presentation of a Mass in Central Abdomen

- There is a mass in central abdomen, 3 × 4 cm, smooth (or irregular), nontender (or tender), ill-defined margin (or round margin), soft in consistency, and freely movable from underlying structure and overlying skin.

Causes of mass in central abdomen (according to the age and sex):

If the patient is young or early-aged, the causes are:

- Lymphoma.
- Tuberculosis (tabes mesentericus or lymphadenitis).
- Hydatid cyst.
- Mesenteric cyst.
- In female, ovarian cyst and pregnancy.
- Distended urinary bladder (urinary retention).

If the patient is elderly or middle-aged, the causes are:

- Intra-abdominal malignancy.
- TB (tabes mesentericus or lymphadenitis).
- Lymphoma.
- Metastatic lymphadenitis.
- Hydatid cyst.
- Mesenteric cyst.
- Retroperitoneal growth (sarcoma).
- Distended urinary bladder (urinary retention).

Q: Suggest one investigation that will help in the diagnosis.

A: USG of whole abdomen.

Q: Suggest one investigation that will confirm the diagnosis.

A: CT-guided or USG-guided FNAC.

Q: What investigations do you suggest?

A: As follows (according to suspicion of cause):

- USG (investigation of choice).
- Hb%, TC, DC and ESR.
- If TB is suspected, MT, chest X-ray PA view.
- CT or MRI.
- FNAC (CT-guided or USG-guided).
- Barium enema (double-contrast) or barium meal and follow-through or small bowel enema (Ryle tube is introduced through mouth and barium is given).
- Colonoscopy.
- Laparoscopy and biopsy (if needed) or laparotomy (in some cases).
- If palpable lymph node, FNAC or biopsy is required.
- If hydatid cyst suspected, Casoni test, haemagglutination test.

Presentation of a Mass in Lower Abdomen (Hypogastrium)

- There is a mass in lower abdomen, 8 × 8 cm, smooth (or irregular), nontender (or tender), regular margin (or round margin), soft in consistency, and freely movable from underlying structure and overlying skin.

Q: What are the causes of mass in lower abdomen?

A: As follows (mention according to your findings, considering the age and sex of the patient):

- In female: Pregnancy in young, fibroid uterus, ovarian cyst or other ovarian mass (e.g. carcinoma).
- Retention of urine.
- Carcinoma of urinary bladder.
- Intra-abdominal malignancy, lymphoma.

Q: What investigations do you suggest?

A: Investigation should be done according to the history and physical findings. Most important is USG.

Presentation of Renal Mass (or Mass in Flank)

- There is a mass in left flank, 3 × 4 cm, smooth (or irregular), nontender (or tender), ill-defined margin (or round margin), soft in consistency, and freely movable from underlying structure and overlying skin.

Q: What are the causes of unilateral renal mass?

A: As follows:

- Renal cell carcinoma (middle-aged or elderly), Wilms tumour (in children).

- Unilateral hydronephrosis or pyonephrosis.
- Hypertrophied single kidney (if nephrectomy of other kidney).
- Large renal cyst.
- Polycystic kidney with single palpable kidney (due to asymmetrical enlargement).
- Right kidney may be normally palpable.

Q: What are the causes of bilateral renal mass?

A: As follows:

- Polycystic kidney disease.
- Bilateral hydronephrosis.
- Diabetic nephropathy in early stage.
- Amyloidosis.
- Rarely, bilateral renal cell carcinoma.

Carcinoma of Stomach

Instruction by the examiner:

- Examine the abdomen.
- Palpate the abdomen.

Presentation of a Case

- There is a mass in epigastric region, 9 × 7 cm, irregular, nontender, margin is ill-defined, firm in consistency and not freely movable.

My **differential diagnoses** are:

- Carcinoma of stomach.
- Hepatoma or secondaries in the liver.
- Lymphoma of stomach.
- Carcinoma of head of the pancreas.
- Carcinoma of transverse colon.
- Pancreatic pseudocyst.

Q: What **else** do you like to see?

A: I want to palpate left supraclavicular gland (Virchow gland, called Troisier sign). If carcinoma of the stomach, there may be metastasis to left suprarenal lymph node.

Q: Suggest one **investigation**.

A: Ultrasonography (this will show the nature of the mass, whether from the stomach, liver, pancreas, etc.).

Q: Mention **one investigation** to confirm carcinoma stomach.

A: Endoscopy and biopsy.

Q: What are the **presentations** of carcinoma of stomach?

A: As follows:

1. Any patient above 40 years of age presenting with '**three As**' (Anaemia, Anorexia, Asthaenia).
2. Vomiting (if tumour in the pyloric end).
3. Pain in the epigastrium.
4. Dysphagia (if tumour in the cardiac end).
5. Haematemesis and melaena.
6. Mass in the epigastrium.
7. Only unexplained features of anaemia.
8. Features of metastasis:
 - Hepatomegaly.
 - Virchow gland.
 - Hard nodule around umbilicus (Sister Mary Joseph nodule).
 - Ovarian involvement (Krukenberg tumour).
 - Prerectal pouch: A shelf-like mass (Blumer shelf).
9. Paraneoplastic syndrome (acanthosis nigricans, dermatomyositis, thrombophlebitis migrans).



Virchow gland (left)

Q: What are the **types** of carcinoma stomach?

A: As follows:

1. Macroscopic observations show four types:
 - Polypoid.
 - Ulcerative.
 - Fungating or cauliflower.
 - Diffuse infiltrative (linitis plastica, rare).
2. Microscopic observation shows two types:
 - Adenocarcinoma (95%) in turn has two types:
 - Intestinal, arising from areas of intestinal metaplasia (more common, with better prognosis)

- Diffuse, arising from normal gastric mucosa (poorly differentiated, occurs in younger age and bad prognosis).
- Others are squamous cell carcinoma, non-Hodgkin lymphoma and leiomyosarcoma.

Q: What are the **causes** or **predisposing factors** for carcinoma stomach?

A: Causes are unknown. Predisposing factors are:

1. Diet:
 - Preservatives in diet such as nitrites and nitrates convert to *N*-nitroso compounds, which are carcinogenic. Nitrate is converted by nitrite-reducing bacteria, which colonize in achlorhydric stomach.
 - Diet rich in salted, smoked or prickled food.
 - Diet lacking fresh fruits, vegetables and vitamins C and A may be the contributing factors (diet with high amount of vegetables and fruits and with low salt protects carcinoma stomach).
2. Smoking.
3. Alcohol.
4. Gastric surgery (partial gastrectomy and gastrojejunostomy. It is due to intestinal metaplasia and chronic gastritis).
5. Infection by *H. pylori* causes chronic atrophic gastritis and intestinal metaplasia, which is precancerous. This organism is responsible in 60–70% cases, mostly associated with achlorhydria. Chronic inflammation with generation of reactive oxygen species and depletion of antioxidant ascorbic acid are also important.
6. Others include pernicious anaemia, adenomatous gastric polyp, familial adenomatous polyposis, Ménétrier disease, blood group A and first-degree relatives.
7. Rarely, gastric cancer families, in which diffuse gastric cancers occur in association with mutations of E-cadherin gene. It is inherited as autosomal dominant trait.

Q: What are the **sites** of carcinoma stomach?

A: As follows:

- Antrum: 50%.
- Body of stomach (greater curvature): 20–30%.
- Cardiac end of stomach: 20%.

In Western countries, proximal tumours are becoming more common.

Q: What is the **benign tumour** of the stomach?

A: Leiomyoma.

Q: What is **early gastric cancer**?

A: It is defined as 'when carcinoma is confined to mucosa or submucosa regardless of lymph node involvement'.

Q: What is **linitis plastica**?

A: It is the diffuse submucosal infiltration by scirrhous carcinoma. Stomach becomes like a rigid tube (other causes of linitis plastica are lymphoma, sarcoidosis and secondary syphilis).

Q: What **investigations** are done?

A: As follows:

- Hb%, TC, DC and ESR.
- Barium meal double contrast (filling defect, irregular ulcer, in infiltrating type and stomach looks like tube).
- Endoscopy and biopsy.
- USG of whole abdomen (to see any metastasis).
- Stool for occult blood test.
- Gastric lavage for exfoliative cytology (previously done when endoscopy was not available).
- To monitor recurrence, carcinoembryonic antigen may be done.

Q: How to **treat** a case of carcinoma stomach?

A: As follows:

1. Surgery is the only curative treatment. 50-year survival is 90% if surgery is done in early gastric cancer; but only 10% if done in advanced cases.
2. Perioperative chemotherapy: ECF (epirubicin, cisplatin and fluorouracil) has improved 5-year survival in operable gastric and lower oesophageal adenocarcinoma.
3. Chemotherapy—not much helpful. **FAM** (combination of 5-Fluorouracil + adriamycin + mitomycin C) may be tried.
4. Palliative:
 - Radiotherapy: Very-little role.
 - Endoscopic laser ablation of tumour tissue, if surgery is not possible (palliative therapy).
 - Endoscopic dilatation or insertion of expandable metallic stents may be used for relief of dysphagia or vomiting.

Gastric Lymphoma

It is the second commonest neoplasm of stomach. Among the GIT lymphoma, 60% occurs in the stomach. 95% is low-grade non-Hodgkin B-cell type. Gastric lymphoma may be:

- Primary: Arise from mucosa-associated lymphoid tissue (MALT).
- Secondary to lymph node involvement in other parts of the body.

Primary gastric lymphoma may be due to *H. pylori* infection. 85% are low grade and 40% are high grade, when associated with *H. pylori* infection. Chronic antigenic stimulation results in monoclonal lymphoproliferation that may cause low-grade MALT lymphoma.

Symptoms: Similar to that of gastric cancer. Patients with primary gastric lymphoma have stomach pain, ulcers or other localized symptoms; but systemic complaints such as fatigue or fever are rare.

Diagnosis: By endoscopy and biopsy. At endoscopy, the tumour usually appears as a polypoid or ulcerating mass.

Treatment:

- Primary type: Treatment with antihelicobacter therapy may regress the tumour. If no response, other therapy for lymphoma should be given (radiotherapy or chemotherapy).
- Secondary type: Usual therapy for lymphoma (chemotherapy, radiotherapy).

Prognosis: Varies according to type. Features predicting a favourable prognosis are stage I or II disease, small resectable tumour or tumour with low-grade histology, and age below 60 years.

Carcinoma of Head of Pancreas (Mass in the Epigastrium)

Instruction by the examiner:

- Examine the abdomen.
- Palpate the abdomen.

Presentation of a Case

- There is a mass in epigastric region, 7 × 7 cm, irregular, nontender, margin is ill-defined, firm in consistency and not freely movable (the patient is also extremely emaciated).



Carcinoma head of pancreas

My **differential diagnoses** are:

- Carcinoma of stomach.
- Hepatoma or secondaries in the liver.
- Lymphoma of stomach.
- Carcinoma of head of the pancreas.
- Carcinoma of transverse colon.
- Pancreatic pseudocyst.

Q: What **relevant** do you like to see if it is carcinoma of the head of the pancreas?

A: Jaundice, scratch marks for itching; also the patient is emaciated, may be pigmented also.

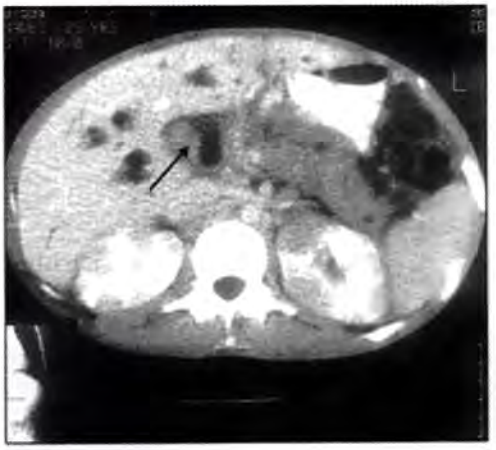
Q: Suggest **one investigation** in this case.

A: USG of upper abdomen.

Q: What **other investigations** do you suggest?

A: As follows:

1. Liver function test (bilirubin, SGPT, alkaline phosphatase, prothrombin time, etc. Alkaline phosphatase is usually very high).
2. CT scan of abdomen.
3. MRI scan and endoscopic ultrasound are helpful in some cases.
4. CT or ultrasound-guided FNAC: May be done; but not in potentially operable case. It may spread the malignancy to the peritoneum.
5. Tumour markers especially CA 19-9 is highly sensitive (80%); but false-positive result may be found.
6. Others:
 - Barium meal X-ray with C-loop (it will show widening of the C-loop).
 - Blood glucose.
 - ERCP (to see obstruction, irregularity or distortion of pancreatic duct. Also, helpful to insert stent in obstructive jaundice.).
 - MRCP may be done.
 - Sometimes laparoscopy and laparoscopic USG (in very small lesion).



Carcinoma head of pancreas

Q: What are the **causes** of carcinoma head of pancreas?

A: Actual causes are unknown. Some factors are responsible:

- Age, above 70 years.
- Male, predominant (twice more than female).
- Chronic pancreatitis.
- Alcohol.
- Smoking.
- Environmental factors, such as petroleum product and naphthylamine.
- Genetic in 5–10% cases. There may be hereditary pancreatitis, multiple endocrine neoplasia (MEN) and hereditary nonpolyposis colon cancer (HNPCC).

Q: What are the **types** of carcinoma of pancreas and the **sites**?

A: Usually adenocarcinoma (90%), which arises from the epithelium of pancreatic duct. Sites are as follows:

- 60% in head.
- 25% in body.
- 15% in tail.

Q: What are the **other tumours** of pancreas?

A: Some tumours may arise from islets cell (insulinoma, gastrinoma, glucagonoma, somatostatinoma, VIPoma, etc.). May occur as a part of MEN I (parathyroid hyperplasia or adenoma, pancreatic tumour, pituitary adenoma).

Q: What are the **presentations** of carcinoma of the pancreas?

A: As follows:

- Painless obstructive jaundice, with palpable gall bladder: In case of carcinoma of head of pancreas.
- Carcinoma involving the body and tail: Usually presents with pain in the epigastrium, deep seated, dull aching, radiates to the back, more on lying flat, feels better with bending forward (pain is due to involvement of coeliac plexus).
- Loss of weight, anorexia, nausea.
- Mass in upper abdomen (in 20% cases).
- Others: Diabetes mellitus, acute pancreatitis.
- Rare features are: Thrombophlebitis migrans (arm vein is more involved than leg vein), venous thrombosis, portal hypertension (due to splenic vein thrombosis) and marantic endocarditis.

N.B. Courvoisier's law: In a jaundiced patient with palpable gall bladder, the cause is unlikely to be gall stones; rather it is due to carcinoma head of pancreas and extrinsic pressure in bile duct. (Reverse of the law: Obstructive jaundice without palpable gall bladder is unlikely to be due to carcinoma head of pancreas and extrinsic pressure in common bile duct.)

Q: How to **treat** carcinoma head of pancreas?

A: As follows:

1. In early stage, surgical resection (Whipple operation is performed: In this operation, pancreas, duodenum, draining lymph node and part of mesentery are removed). 5-year survival is 20% after surgery. Survival is improvement with adjuvant chemotherapy (5-FU).
2. Other treatment (usually palliative):
 - Endoscopic insertion of stent to relieve intractable itching.
 - For pain, analgesic, injection of alcohol in celiac plexus (USG-guided or endoscopic-USG-guided).
 - Chemotherapy: 5-FU, adriamycin and cisplatin may be tried. Combination of 5-FU plus gemcitabine may help to improve the survival in advanced disease.
 - Radiotherapy is not much helpful.

Q: What is the **prognosis**?

A: Prognosis is **bad;** mean survival is <6 months. Usual 5-year survival is 2–5%. Following Whipple operation, 5-year survival is 5–14%. If adjuvant chemotherapy is given with 5-fluorouracil, then 5-year survival becomes 21–29%. Prognosis is better if tumour size <3 cm, no lymph node involvement, negative resection of margin at surgery, ampullary or islet cell tumours.

Pancreatic Pseudocyst

Instruction by the examiner:

- Examine the abdomen.
- Palpate the abdomen.

Presentation of a Case

- There is a mass in epigastric region, 7 × 9 cm, irregular, nontender, margin is ill-defined, cystic in consistency and not freely movable.



Pseudocyst of pancreas

My **differential diagnoses** are:

- Carcinoma of stomach.
- Hepatoma or secondaries in the liver.
- Lymphoma of stomach.
- Carcinoma of head of the pancreas.
- Carcinoma of transverse colon.
- Pancreatic pseudocyst.

Q: What are the **presentations** of pancreatic pseudocyst?

A: As follows:

- History of acute pancreatitis, trauma to abdomen.
- Asymptomatic, if small cyst.
- Anorexia, nausea, vomiting, pain abdomen, weight loss and mass in the epigastrium.

Q: What is **pancreatic pseudocyst?** Why it is called **pseudocyst?**

A: It is the localized peripancreatic collection of pancreatic juice and debris, surrounded by granulation tissue, which usually develops in lesser sac following inflammatory rupture of pancreatic duct. It is called pseudocyst because there is no lining epithelium of cyst.

Q: What **investigations** do you suggest?

A: As follows:

- Ultrasonography.
- CT or MRI.
- Serum amylase (persistently high).
- Others (LFTs, blood sugar, urea, creatinine and serum electrolytes).



Pancreatic pseudocyst

Causes of pancreatic pseudocyst:

- Acute pancreatitis, usually 1–2 weeks after acute attack.
- Chronic pancreatitis.
- Trauma.

Treatment of pancreatic pseudocyst:

- Small cyst, <6 cm, no specific treatment and spontaneous resolution may occur.
- For large cyst, conservative treatment, spontaneous resolution in 4–6 weeks.
- If no response or cyst >6 cm, or rapidly enlarging cyst or features of obstruction of bile duct or duodenum, surgery should be done. Cyst is drained to stomach, duodenum or jejunum, after 6 weeks, once pseudocyst is matured.
- Aspiration under USG may be done.

Q: What are the **complications** of pancreatic pseudocyst?

A: As follows:

- Rupture of the cyst.
- Secondary infection and abscess formation.
- Compression of surrounding structures, obstruction of bile duct or duodenum or blood vessels causing pseudoaneurysm.

Mass in the Epigastrium (Aneurysm of Aorta)

Instruction by the examiner:

- Examine the abdomen.
- Palpate the abdomen.

Presentation of a Case

- There is a pulsatile mass in epigastric region, 3 × 4 cm, nontender, margin is well defined, soft in consistency.

My diagnosis is **aneurysm of abdominal aorta.**

Q: What are the **causes** of epigastric pulsation?

A: As follows:

- Normally, in lean and thin person (palpable, but nonexpansile).
- Right ventricular hypertrophy.
- Pulsatile liver (in tricuspid regurgitation).
- Mass overlying aorta (carcinoma of stomach).

To **differentiate** from aneurysm, place two fingers parallel at the outermost palpable margin. If aneurysm is present, pulsation is expansile (see the fingers that go apart from each other and measure the distance).

Q: What are the **causes** of aneurysm?

A: As follows:

- Atherosclerosis (the commonest cause: 90%, commonly abdominal aorta below the origin of renal artery).
- Aortitis due to syphilis (rare now-a-days), Takayasu disease, giant cell arteritis, Reiter syndrome and ankylosing spondylitis.
- Mycotic aneurysm (by *Staphylococcus* and by *Streptococcus* in atheromatous plaque).
- Cystic medial necrosis (in Marfan syndrome, Ehlers–Danlos syndrome).
- Collagen vascular disease.
- Trauma.

Q: What are the **presentations** of abdominal aneurysm?

A: It is three times more in males, above 60 years of age:

- May be asymptomatic.
- Pulsatile mass.
- Intermittent or continuous abdominal pain that radiates to the back, iliac fossa or groin.
- Sometimes, there may be acute severe pain due to rupture and can cause collapse.
- Features of thromboembolism.

Q: What is **aneurysm of signs** and **aneurysm of symptoms?**

A: As follows:

- Aneurysm of signs: When aneurysm involves ascending aorta, there are signs of aortic regurgitation and pulsation in right side of sternum.
- Aneurysm of symptoms: When aneurysm involves aortic arch and descending aorta, there are symptoms due to pressure (dysphagia, hoarseness, stridor and breathlessness).

Q: What are the **complications** of aneurysm?

A: As follows:

- Rupture.
- Thrombosis.
- Embolism.
- Pressure on nearest structure.

Q: What **investigations** do you suggest?

A: As follows:

- USG of abdomen (investigation of choice).
- Plain X-ray of abdomen (curvilinear calcification may be present).
- CT scan.
- Aortography.
- Others to find out risk factors (blood sugar, lipid profile, VDRL and TPHA).

Q: How to **treat** aneurysm?

A: As follows:

- Symptomatic: Surgery should be done.
- Asymptomatic, but aneurysm >5.5 cm: Surgery (because of risk of rupture).
- Small aneurysm: Follow-up (by serial USG).

Q: What is **dissecting aneurysm**? What are the **types**?

A: It means when there is a tear in intima of aorta, exposing diseased media to blood and creating a false lumen. It is of two **types**:

- Type A: When involves ascending aorta; may extend to involve descending aorta.
- Type B: When involves descending aorta, below the left subclavian artery.

Causes of dissecting aneurysm:

- Hypertension, the commonest cause (80%).
- Cystic medial necrosis in aortic wall (Marfan syndrome and Ehlers–Danlos syndrome).
- Surgery (aortic valve replacement and coronary artery bypass surgery).
- Pregnancy (in the third trimester).

Presentations:

- Sudden severe chest pain, tearing in nature, between shoulder blades.

- Features of shock.
- Features like acute myocardial infarction.
- Asymmetrical pulse, features of AR.
- Chest X-ray (widening of upper mediastinum).
- Echocardiogram (transoesophageal echocardiogram highly specific).
- CT or MRI (also highly specific).

Treatment:

- When it involves ascending aorta, immediate surgery is suggested.
- When it involves descending aorta, conservative treatment is suggested; surgery may be necessary later on.
- Treatment of primary cause (BP must be controlled).

Mass in Right Iliac Fossa (Ileocaecal Tuberculosis)

Instruction by the examiner:

- Examine the abdomen.
- Palpate the abdomen.

Presentation of a Mass in Right Iliac Fossa

- There is a mass in right iliac fossa, 4 × 6 cm, surface is irregular, nontender, ill-defined margin, firm in consistency, and freely movable from underlying structure and overlying skin.

My differential diagnoses are (tell the causes according to the age of the patient):

If the patient is young or early-aged:

- Appendicular lump (usually tender).
- Ileocaecal tuberculosis.
- Crohn disease.
- Lymphoma.
- Tubo-ovarian mass in female.
- Others: Pelvic kidney, tumour in undescended testes.

If the patient is elderly or middle-aged:

- Appendicular lump (usually tender).
- Ileocaecal tuberculosis.
- Carcinoma of caecum (usually hard, irregular and nontender).
- Lymphoma.

N.B. If there is scar mark in lumbar area, diagnosis is transplanted kidney.

Q: Mention **one investigation.**

A: Ultrasonography of abdomen.

Q: What are the **causes** of ileocaecal TB? Or what is the **pathogenesis?**

A: It is caused by reactivation of primary disease by *Mycobacterium tuberculosis*. May be secondary to pulmonary TB (by swallowing of sputum). Sometimes, primary TB due to *Mycobacterium bovis* (rare now-a-days). After involvement of mucosa and submucosa, intense inflammation with necrosis occurs in the bowel wall and lymphatic. Caseation often found.

Q: What is the **type of lesion** and **type of ulcer** in ileocaecal TB?

A: Types of lesions are ulcerative, hypertrophic or mixed. Ulcer is transverse (in typhoid and Crohn disease, and ulcer is longitudinal).

Q: What are the **presentations** of ileocaecal TB?

A: History of pulmonary TB may be present:

- Abdominal pain is the commonest (usually in right iliac fossa, occasionally generalized).
- Features of intestinal obstruction (acute or subacute), or peritonitis or ascites.
- Diarrhoea or malabsorption syndrome.
- Mass in right iliac fossa.
- Others are fever, malaise, loss of weight and fistula formation.

Q: What investigations are done to **diagnose** ileocaecal TB?

A: As follows:

- CBC and ESR.
- Chest X-ray (shows TB in 50%).
- Mantoux test (MT).
- USG of abdomen.
- CT scan.
- Barium follow-through with spot film in ileocaecal region.
- Colonoscopy or ileoscopy may be done.
- Sometimes, laparoscopy to see tubercle in peritoneum and biopsy.

Q: What are the **complications** of ileocaecal TB?

A: As follows:

- Intestinal obstruction.
- Fistula (enteroenteric or enterocutaneous).
- Malabsorption.
- Perforation (rare).

Q: What is the **treatment** of ileocaecal TB?

A: As follows:

- Standard anti-TB chemotherapy (using four drugs) for 1 year.
- Occasionally, surgery (if intestinal obstruction or fistula).

Crohn Disease

Instruction by the examiner:

- Examine the abdomen.
- Palpate the abdomen.

Presentation of a Mass in Right Iliac Fossa

- There is a mass in right iliac fossa, 2 × 3 cm, surface is irregular, nontender, margin is ill-defined, firm in consistency, and freely movable from underlying structure and overlying skin. (There may be multiple scar in abdomen due to repeated surgery or fistula.)

My differential diagnoses are: As in ileocaecal tuberculosis.

Q: What are the causes of multiple fistula or sinuses in abdominal wall?

A: As follows:

- Trauma.
- Crohn disease.
- Abdominal tuberculosis.
- Faecal fistula.
- Actinomycosis.
- Disseminated malignancy.

Q: What are the **sites** of Crohn disease?

A: Any part of gastrointestinal tract, from mouth to anus, may be involved, but commonly terminal ileum is involved (hence, it was previously called regional ileitis). In order of frequency, ileum and right side of colon, colon alone, terminal ileum alone, ileum and jejunum. Lesion is transmural (all layers are involved). The disease can involve a small area of the gut, or multiple areas with relatively normal bowel in between them called 'skip lesion'.

Q: What is Crohn disease? What are the presentations?

A: Crohn disease is a chronic inflammatory disease of unknown aetiology involving any part of gastrointestinal tract, commonly the terminal ileum. It is slightly common in female, M:F = 1:1.2, more in young (mean age is 26 years). Common presentations are as follows:

- Frequent diarrhoea.
- Abdominal pain (colicky).
- Weight loss.
- Failure to thrive in children.
- Other systemic features are malaise, lethargy, low-grade fever, anorexia, nausea, vomiting.
- Extraintestinal manifestations (see below).
- Sometimes, it may present with acute emergency (e.g. acute appendicitis). If laparotomy is done, terminal ileum looks oedematous and red.
- Sometimes, the patient may present with recurrent aphthous ulceration of mouth, mass in right iliac fossa (due to inflamed loops of bowel matted together or abscess), anal fissures or perianal abscess.

Q: What are the causes of Crohn disease?

A: Actual causes unknown. Probable factors are:

- Genetic and familial.
- Diet: High sugar and fat, but low residue diet.
- Smoking.
- Probable association with mycobacteria and measles virus (not proved).
- Abnormal immunological response.

N.B. Remember the following points:

- Appendicectomy is protective of ulcerative colitis, but may increase the risk of Crohn disease or may result in more aggressive disease.
- Oral contraceptive pill increases the risk of Crohn disease.

Extraintestinal manifestations of Crohn disease

- **Eyes:** Conjunctivitis, episcleritis, uveitis or iritis.
- **Mouth:** Aphthous ulcer and thickened lip.
- **Skin:** Erythema nodosum, pyoderma gangrenosum, fistula or scar in abdominal wall.

- **Bones and joints:** Acute arthropathy or arthralgia, ankylosing spondylitis or sacroiliitis and clubbing.
- **Perianal region**: Perianal fistula, skin tag and abscess.
- **Liver or hepatobiliary:** Fatty liver, pericholangitis, sclerosing cholangitis (common in ulcerative colitis), autoimmune hepatitis, cirrhosis of liver, granuloma, liver abscess or portal pyaemia, gall stone and cholangiocarcinoma.
- **Kidney:** Nephrolithiasis (oxalate stone), hydronephrosis and pyelonephritis.
- **Others:** Amyloidosis and venous thrombosis.

Q: What is the relation of **smoking** in IBD?

A: In smokers, the incidence of Crohn disease is high. But there is increased risk of ulcerative colitis in nonsmokers or ex-smokers.

Q: What are the types of **arthritis** in Crohn disease?

A: Peripheral arthropathy is common, which may be of two types:

- Type 1, Pauciarticular: Usually acute, self-limiting, <10-weeks duration, occurs with IBD relapses, usually associated with other extra-intestinal features of IBD. Indicates active disease.
- Type 2, Polyarticular: Lasts longer (months to years), not related to IBD activity; usually associated with uveitis.

Other types are: Ankylosing spondylitis, arthralgia, inflammatory back pain, which are not related to IBD disease activity.

Q: What are the **differential diagnoses** of Crohn disease?

A: As follows:

- Acute appendicitis or appendicular lump.
- Ileocaecal TB.
- Carcinoma of caecum.
- Lymphoma.
- Amoeboma.
- Mesenteric adenitis.
- Infections by *Yersinia*, actinomycosis.

Q: How to assess the **activity** of Crohn disease?

A: Signs of activity are:

1. Clinical:
 - Eye signs: Episcleritis, conjunctivitis and iritis.
 - Mouth: Aphthous ulcer.
 - Skin: Erythema nodosum and pyoderma gangrenosum.
 - Arthralgia of large joints.
 - Fatty liver or liver abscess or portal pyaemia.
 - Mesenteric or portal vein thrombosis.
 - Venous thrombosis (in other veins).
2. Morphology: By radiological or endoscopy.
3. Laboratory:
 - Low albumin (due to protein-losing enteropathy).
 - High ESR.
 - High C-reactive protein (CRP).
 - Scanning with white cell labelled with ^{111}Indium or ^{99m}Tc to locate active site.

Q: What **investigations** should be done in Crohn disease?

A: As follows:

- CBC (anaemia is normocytic, may be megaloblastic due to vitamin B_{12} deficiency).
- ESR and CRP (both high).
- Total protein and A:G ratio (low albumin).
- Liver function tests (may be abnormal).
- Blood for C/S (if septicaemia is suspected).
- Stool for R/E and C/S (to exclude infective cause like salmonella, shigella, campylobacter, *E. coli*, *Clostridium difficile*).
- USG of whole abdomen.
- Barium follow-through or small bowel enema (detects ileal disease; there may be narrowing of the affected segment called string sign, which is pathognomonic of Crohn disease).
- Barium enema.
- Colonoscopy (in colonic Crohn disease) with ileoscopy and biopsy.
- Enteroscopy.
- Capsule endoscopy (in assessing small bowel disease).
- CT scan or MRI of abdomen.

Q: How to **treat** Crohn disease?

A: Induction of remission in active disease and maintenance of remission.

1. Induction of remission:
 a. General measures:
 - Diet, with high protein, low fat and milk free. If needed, enteral or parenteral feeding.
 - For anaemia: Supplement of iron, B_{12}, folic acid and zinc. Erythropoietin may be given.
 - Symptomatic treatment for diarrhoea (loperamide, codeine phosphate or cophenotrope). In longstanding diarrhoea, cholestyramine may be helpful.

 b. Drugs:
 - Prednisolone: 40–60 mg/day. Budesonide may be used in moderately active disease.

- Combination of prednisolone and azathioprine or 6-mercaptopurine (6-MP) may be used.
- For perianal disease, metronidazole (400 mg BD for 14 days) **plus** ciprofloxacin may be given. 6-MP or azathioprine may be used in chronic case. Infliximab and adalimumab are effective in healing fistula and perianal disease.
- In active and moderate-to-severe total Crohn colitis or ileo-colitis, treatment is like active ulcerative colitis, as follows:
 - Oral and per-rectal aminosalicylate plus per-rectal steroid should be given.
 - Oral prednisolone is indicated for more active disease or when aminosalicylate is ineffective.
 - In more severe colitis or in patient who fails to maximum oral therapy, patient should be hospitalized and treated as follows:
 - IV fluid and nutritional support.
 - IV methyl prednisolone or hydrocortisone 100 mg 6 hourly.
 - Topical and oral aminosalicylates are also used.
 - If the patient does not respond to the steroid therapy, then IV cyclosporine or infliximab may be given. Otherwise urgent surgery should be done.

2. Maintenance of remission:
 - Smoking must be stopped.
 - Aminosalicylates may be given, but has minimal efficacy.
 - Thiopurines (azathioprine or 6-MP) is given in patient who relapses more than once a year.
 - If it fails, weekly MTX should be given.
 - In aggressive disease, combination of immunosuppressive and anti-TNF therapy should be given.
3. In resistant cases (to steroid or immunosuppressive) or failure of above therapy, the following treatment may be given:
 - Methotrexate.
 - IV cyclosporine.
 - Anti-TNF antibody, e.g. infliximab may be given in infusion 4–8 weekly, in three occasions. Also, adalimumab may be used. Relapse usually occurs after 12 weeks. So, MTX or azathioprine or 6-MP should be added to maintain remission (etanercept is ineffective). Infliximab helps in healing fistula and perianal disease. These agents are contraindicated in presence of infection including tuberculosis. Allergic reaction may occur.
4. Surgical management: Surgery should be avoided, if possible, and only minimum resection should be done, as the disease is multicentric and recurrence is almost inevitable. Indications of surgery are:
 - Failure of medical therapy, intractable disease or fulminant disease.
 - Complications like toxic megacolon, obstruction, perforation, massive haemorrhage, refractory fistula and abscess, etc, which are not responding to medical treatment.
 - Extra-intestinal complications like severe arthritis or pyoderma gangrenosum not responding to medical treatment.
 - Failure to grow in children despite medical treatment.
 - Suspicion of malignancy or severe dysplasia.

 Recurrence is common after surgery. If second surgery is needed, azathioprine or 6-MP should be added to prevent the chance of recurrence. There is no strong benefit, if it is given after first surgery.

N.B. Prednisolone has no role to prevent recurrence.

Q: What are the differences between ulcerative colitis and Crohn disease?

A: As follows:

Features	Crohn disease	Ulcerative colitis
Site	Mouth to anus, commonly ileum and right side of colon	Large gut, commonly rectum
Nature	Transmural (all layers of gut wall are involved)	Mucosa
Type	Patchy and discontinuous, skip lesions are present	Continuous or confluent
Crypt abscess	Less	Common
Fistula, perianal or ischiorectal abscess, and skin tag	Common	Uncommon
Others	Deep ulcers with fissure. Mucosa in between them looks like cobblestone	Pseudopolyps (hypertrophy of mucosa)

Colon cancer	Less	Common
Microscopy:		
• Granuloma	• In 50–60% cases, noncaseating granuloma present.	• Absent
• Goblet cells	• Slight loss or normal	• Loss or depleted and distorted
• Cells	• Chronic inflammatory cells with lymphoid hyperplasia	• Acute and chronic inflammatory cells in lamina propria and crypts
Smoking	Common in smoker	Common in nonsmoker and ex-smoker

Carcinoma of Colon

Instruction by the examiner:

- Examine the abdomen.
- Palpate the abdomen.

Presentation of a Case

- There is a mass in left iliac fossa, 3 × 4 cm, irregular, nontender, ill-defined margin, hard in consistency and fixed.

My differential diagnoses are (mention according to the age of the patient):

If the patient is young, the causes are:

- Thick colon (in irritable bowel syndrome).
- Faecal mass (mass indented and moulded by pressure).
- Diverticulitis.
- Occasionally, normal colon may be palpable.
- Tubo-ovarian mass in female.
- Pelvic kidney.
- Carcinoma of colon (rare).

If the patient is elderly, the causes are:

- Faecal mass.
- Diverticulitis (tender, mobile mass).
- Carcinoma of colon (descending or sigmoid colon).
- Thick colon (in irritable bowel syndrome).

Q: What **investigations** do you suggest in this case?

A: As follows:

- USG of whole abdomen.
- Stool for occult blood.
- Barium enema (double-contrast).
- Sigmoidoscopy and biopsy.
- FNAC (CT-guided or USG-guided).
- Laparoscopy, in some cases.
- Occasionally, laparotomy may be needed.

Q: What are the **sites** of colorectal carcinoma?

A: As follows:

- Rectum (20%).
- Rectosigmoid (10%).
- Sigmoid colon (25%).
- Caecum and ascending colon (25%).
- Transverse colon (15%).
- Descending colon (5%).

Q: What is the **most common site** of carcinoma of colon?

A: Rectosigmoid (65% cases) is the most common site.

Q: What are the **types** of carcinoma of colon?

A: As follows:

1. Macroscopically:
 - Polypoid and fungating.
 - Annular and constricting.
2. Microscopically: Adenocarcinoma.

Q: What are the **causes** or **predisposing factors** for carcinoma of colon?

A: The causes are unknown. Predisposing factors are as follows:

1. Dietary factors:
 - Excess consumption of red meat, saturated animal fat.
 - Less dietary fibres.
 - Less intake of vegetables and fruits (high vegetables and fruits may be preventive for carcinoma).
 - Excess and prolonged sugar consumption.
2. Nondietary factors:
 - Increasing age.
 - Genetic factors such as benign adenomatous polyp or familial adenomatous polyposis.
 - Hereditary nonpolyposis colonic cancer.
 - Family history of colon cancer.
 - Longstanding extensive ulcerative colitis or Crohn colitis, especially if associated with primary sclerosing cholangitis.

- Personal history of breast cancer.
- Ureterosigmoidostomy.
- Acromegaly.
- Pelvic radiotherapy.
- Alcohol (weak association)
- Smoking (relative risk 1.5–3.0).
- Obesity and sedentary lifestyle.
- Cholecystectomy.
- Type 2 diabetes (hyperinsulinaemia).

Factors that **decrease risk** of colorectal carcinoma:

- Diet: Increased fibre, fruits, vegetable, garlic, milk.
- Exercise (colon only).
- Drugs: Aspirin or other NSAIDs, calcium, folic acid, omega-3 fatty acids, combined oestrogen and progesterone hormone replacement therapy.

Q: What are the features of carcinoma of colon?

A: The features of carcinoma of colon depend on the site (may be asymptomatic):

- If on the left side, there may be bleeding per rectum, alteration of bowel habit, mass in left iliac fossa.
- If on the right side, there may be alteration of bowel habit, intestinal obstruction, mass in right iliac fossa.

N.B. Any patient over 40 years of age presenting with new large bowel symptoms should be investigated. Alarming symptoms are change in bowel habit, rectal bleeding, anorexia and weight loss, faecal incontinence, tenesmus and passing mucus per rectum.

Q: What investigations should be done in colorectal carcinoma?

A: As follows:

- USG of whole abdomen (to see the mass, metastases, lymph node involvement).
- Sigmoidoscopy or colonoscopy and biopsy (gold standard).
- CT colonography.
- CT scan of whole abdomen.
- Endoanal ultrasound or pelvic MRI (used for staging of rectal cancer).
- PET scan is useful for detecting occult metastases and for evaluation of suspicious lesions found on CT or MRI.
- Barium enema (double contrast): May be helpful to see the mass, but CT colonography is more preferable.
- Others: Complete blood count, stool for occult blood, CEA (to see recurrence), X-ray chest.
- FNAC (CT-guided or USG-guided).
- Sometimes, laparotomy may be needed.

Q: How screening and prevention are done in carcinoma of colon?

A: Screening is done in the following way:

- Any person >50 years of age, stool is tested for the presence of occult blood.
- Colonoscopy (gold standard).
- Flexible sigmoidoscopy is an alternative to colonoscopy.
- CT colonoscopy may be used in screening programme.
- Screening for high-risk patients by molecular genetic analysis (very promising, but not widely available).

Prevention:

- Chemoprevention by using aspirin, calcium, folic acid. Cox-2 inhibitor may have some role to play in prevention.
- Secondary prevention to detect early and precancer stage. It is done by screening.

N.B. Remember the following:

- Colorectal carcinoma is common in the Western world, less among Asians.
- Second common cause of death.

Q: How the colorectal carcinoma spreads?

A: As follows:

- Local infiltration through bowel wall.
- By lymphatics.
- By blood.
- Transcoelomic.

Q: How to treat colorectal carcinoma?

A: As follows:

1. Curative:
 - Surgical resection of the tumour with pericolic lymph nodes.
 - Adjuvant postoperative chemotherapy (with 5-fluorouracil and folinic acid).
 - Radiotherapy is not much helpful. Preoperative radiotherapy may be given to large fixed rectal cancer to make it resectable. Postoperative radiotherapy may be required in some cases.
 - In some cases with metastatic disease, monoclonal antibodies like bevacizumab or cetuximab, either alone or with chemotherapeutic agents such as irinotecan, may be used.
2. Palliative:
 - Palliative chemotherapy with 5-FU may improve survival. If this fails, second-line drug such as irinotecan may be given.
 - Endoscopic laser therapy or insertion of an expandable metal stent can be used to relieve obstruction.

CHAPTER 5

HAEMATOLOGY

"... it clearly appears that the blood is the generative part, the fountain of life, the first to live, the last to die, and the primary seat of the soul"

– William Harvey

Generalized Lymphadenopathy (Hodgkin Lymphoma)

Usual instructions by the examiner:

- Perform the general examination.
- Examine the neck and relevants.

Presentation of a Case

- Present as described in **generalized lymphadenopathy.**

Q: What is **lymphoma?**

A: Group of disorders due to neoplastic proliferation of lymphoid tissue. Majority are of B-cell origin. The two types are:

- Hodgkin disease (HD).
- Non-Hodgkin lymphoma (NHL).



Right sided cervical lymphadenopathy



Bilateral cervical lymphadenopathy

Q: What is **Hodgkin disease?**

A: It is a type of lymphoma characterized by painless, progressive enlargement of LNs associated with **Reed–Sternberg giant cell** (hallmark of the disease). It usually occurs in adolescence and young adults (20–35 years of age); also after 45 years of age (50–70 years, two peaks of incidence). Median age is 31 year. More in males than females (1.5:1): Three times more with past history of infectious mononucleosis.

Q: What is **Reed–Sternberg cell?**

A: It is a malignant cell of B-cell origin that is characterized by:

- Large cell with paired mirror image nuclei that resembles 'Owl's-eye' appearance.
- Prominent nucleoli.

Reed–Sternberg cell is the hallmark of Hodgkin disease. Rarely, found in infectious mononucleosis, recurrent Burkitt lymphoma and chronic lymphocytic leukaemia (CLL).

Q: What are the types of Hodgkin disease?

A: There are two types of Hodgkin disease:

1. Nodular lymphocyte-predominant Hodgkin lymphoma (HL) (5%, slowly growing, localized and rarely fatal).
2. Classical HL, which is of four types:
 - Nodular sclerosis (70%, common in young, female).
 - Mixed cellularity (20%, common in elderly, male).
 - Lymphocyte predominance (5%, common in men).
 - Lymphocyte depleted (rare, probably represents large cell or anaplastic NHL).

Q: How does the patient present in Hodgkin disease?

A: As follows:

- Asymptomatic.
- Generalized lymphadenopathy starting in cervical glands; then axillary, inguinal, which are painless, discrete and rubbery.
- Dry cough, shortness of breath (due to mediastinal lymphadenopathy).
- Systemic features: Fever, loss of weight, malaise, weakness and pruritus (10%).
- After alcohol intake, pain at the site of LN involvement.

Q: What is Pel–Ebstein fever?

A: Recurrent bouts of pyrexia followed by apyrexial period. May occur in 10% cases of HD.

Q: What are the stages of HD?

A: Ann Arbor staging classification is given below:

- Stage 1: Involvement of single LN region (I) or extralymphatic site (IAE).
- Stage 2: Involvement of two or more LN regions (II), or an extralymphatic site and LN regions on the same side of diaphragm (IIE).
- Stage 3: Involvement of LN regions on both sides of diaphragm with **(IIIE)** or without **(III)** localized extralymphatic involvement or involvement of spleen (IIIS) or both (IIISE).
- Stage 4: Diffuse involvement of one or more extralymphatic tissue with or without LN involvement (bone marrow, liver and lung).

(Lymphatic structures include LN, spleen, thymus, Waldeyer ring, appendix and Peyer patch.)

In the presence of systemic features, each stage may be divided into two:

1. A—No systemic features.
2. B—With systemic features, such as:
 - Weight loss.
 - Drenching sweats.

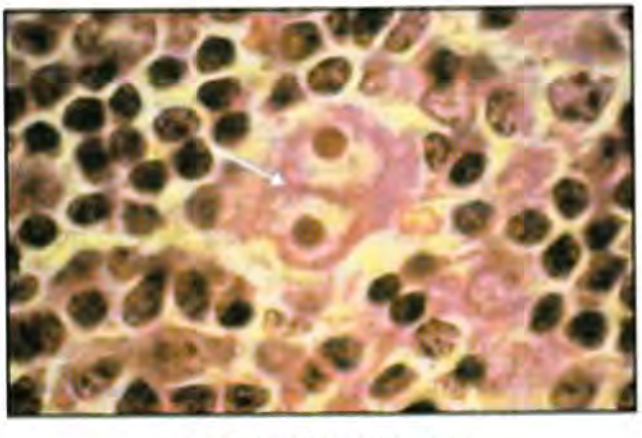
Q: What investigations are done in HD?

A: As follows:

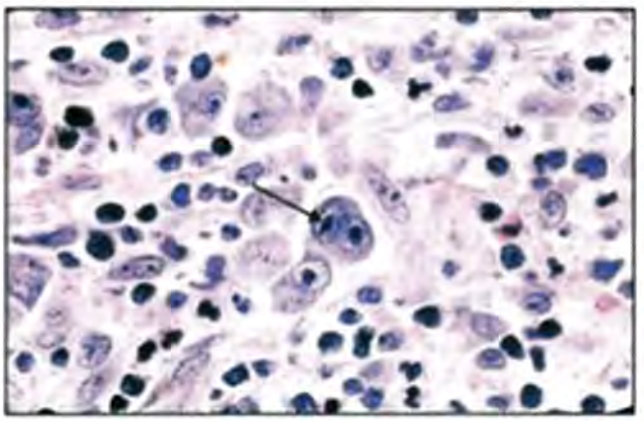
1. CBC: There may be normocytic normochromic anaemia, lymphopaenia, high eosinophil and high ESR. Blood count may be normal.
2. Chest X-ray (shows bilateral hilar lymphadenopathy and widening of mediastinal shadow).
3. FNAC or biopsy (Biopsy is more preferable to see the architecture of lymph node that may not be detected by FNAC; also biopsy is necessary for staging.)
4. Ultrasonography (USG) of whole abdomen.
5. CT scan of chest and abdomen including pelvis (necessary for staging).
6. Others:
 - PET (positron emission tomography): Used for staging, assessment of response and direction of therapy.
 - Bone marrow study (involved in advanced stage).
 - Renal function tests: Mainly creatinine (necessary prior to treatment).
 - Liver function tests: Mainly SGPT (necessary prior to treatment).
 - Serum uric acid (necessary prior to treatment).
 - Serum lactate dehydrogenase (LDH).

N.B. Remember the following points:

- Lymphopaenia, high LDH and lymph node >10 cm are poor prognostic factors.
- High ESR is an indicator of disease activity.
- High alkaline phosphatase (biliary obstruction) indicates involvement of lymph nodes in porta hepatis.



Reed–Sternberg giant cell



Reed–Sternberg giant cell

Q: How is **staging** done and why?

A: For staging, following tests are done:

- Chest X-ray.
- Bone marrow.
- USG of whole abdomen.
- CT scan (whole abdomen and chest).

Staging is done for selection of therapy (radiotherapy or chemotherapy) and prognosis.

Q: How to **treat** HD?

A: As follows:

1. Majority of HD patients are now treated with chemotherapy and adjunctive radiotherapy. ABVD (Adriamycin or doxorubicin, Bleomycin, Vinblastine and Dacarbazine) regimen is widely used. ABVD chemotherapy can cause cardiac and pulmonary toxicity due to doxorubicin and bleomycin, respectively. Infertility and secondary myelodysplasia or acute myeloid leukaemia (AML) is low with this regime.
2. Patient with early stage HD (IA, IIA, no bulk) is treated with 2–4 cycles of ABVD followed by radiotherapy (20–30 Gy) to the involved lymph nodes. Treatment response is monitored by CT scan or positron emission tomography (PET) scan.
3. Patient with advanced disease is usually treated with chemotherapy alone. Usually 6–8 cycles of ABVD is given. Radiotherapy at the bulk site used previously is now avoided. Achieving PET-negative remission predicts a better long-term remission rate. Overall, the long-term disease control or cure rates are lower with advanced disease.
4. New regimens are being tested for those who fail with above therapy (about 25%). This includes BEACOPP (bleomycin, etoposide, adriamycin or doxorubicin, cyclophosphamide, oncovin or vincristine, procarbazine, prednisolone).
5. Patient who is resistant to chemotherapy may be considered for autologous bone marrow transplantation.

Other chemotherapeutic regimen that was previously used is as follows:

- MOPP: Mechlorethamine, oncovin (vincristine), procarbazine and prednisolone.
- COPP: Cyclophosphamide, oncovin (vincristine), procarbazine and prednisolone.

Q: What is the **prognosis** of HD?

A: Prognosis depends on the stage:

- Early-stage HD: Complete remission in >90% when treated with chemotherapy followed by radiotherapy. The majority are cured.
- Advanced-stage HD: 50–70% can be cured.
- Patients who fail to respond to initial chemotherapy have a poor prognosis, but some may achieve long-term survival after autologous bone marrow transplantation.
- Patients relapsing within a year of initial chemotherapy have a good salvage rate with autologous BMT.
- Patients relapsing after 1 year may obtain long-term survival with further chemotherapy alone.
- Presence of B symptoms indicate adverse prognosis.

N.B. Remember the following points:

- Fertility is usually preserved after radiotherapy.
- In young women with mediastinal disease, radiotherapy to the breast may cause breast cancer (hence, needs follow-up).
- Patients who continue to smoke after chest radiotherapy, lung cancer may occur.
- Cardiac disease may occur after supradiaphragmatic mantle field radiation.
- After chemotherapy, infertility may occur in man (needs counselling and storage of sperm).
- Infertility is less in woman. Premature menopause may occur.
- In 5%, myelodysplasia and acute leukaemia may occur 5–10 years after alkylating agent.

Q: What is **disease-free** or **cure** in HD?

A: If no relapse after 5 years of withdrawal of treatment, it is called cure or disease-free.

Generalized Lymphadenopathy (Non-Hodgkin Lymphoma)

Instructions by the examiner:

- Perform general examination.
- Examine the neck and relevant.

Q: What is **non-Hodgkin lymphoma (NHL)**? What are the **types (grading)**?

A: NHL refers to malignant proliferation of lymphoid cells; and majority is B-cells (70%) and few T-cells (30%).

Types or grading (depending on the rate at which the cells are dividing):

- **Low grade** shows the following characteristics:
 - Low cell proliferation rate.
 - Asymptomatic for many years.
 - Slow indolent course.
 - Remitting and relapsing course.
 - Good response to minimal therapy.
 - Incurable, but the patient survives for long time.
 - Most nodular lymphoma is of low grade.
 - Small-cell disease (mature lymphocyte) is associated with low-grade lymphoma.
 - No treatment is required, if the disease is not advanced and asymptomatic.
 - Median survival up to 10 years.
 - Transformation to high grade is associated with poor prognosis.
- **High grade** shows the following characteristics:
 - Cell divisions occur quickly.
 - Early symptoms are common.
 - Fatal, if untreated.
 - Responds better to treatment and patient may achieve a long-term remission if treated properly (potentially a curable disease).
 - 80% respond to initial therapy, and 35% are disease-free for 5 years.
 - Large-cell disease (immature lymphoid cells) is of high grade.
 - Most diffuse lymphomas are of high grade.

Stages of NHL are much similar to Hodgkin lymphoma (HL).

Q: What are the **causes** of NHL?

A: Actual cause is unknown. Probable causes are:

- Specific lymphoma types are associated with **Epstein-Barr virus** (EBV), human herpes virus 8 (HHV-8) and human T-cell lymphotropic virus (HTLV) infection.
- *Helicobacter pylori* is an aetiological factor in gastric MALT lymphoma.
- A late manifestation of HIV infection. Primary brain lymphoma, immunoblastic diffuse large B-cell lymphoma and Burkitt lymphoma may occur in AIDS.
- Lymphoma occurs in congenital and acquired immunodeficiency states. Acquired immunodeficiency, as a result of organ transplantation, is strongly associated with NHL. These are commonly extranodal and most frequently occur in the first year after transplantation.
- Gastric lymphomas are associated with specific chromosome lesions. The t(14:18) translocation in follicular lymphoma results in the dysregulated expression of the *BCL-2* gene product, which inhibits apoptotic cell death.
- A number of familial cancer syndromes are also associated with NHL.
- In autoimmune disorders, high risk of NHL is reported, e.g. Sjogren syndrome and extranodal marginal-zone lymphoma.
- There may be an association with exposure to pesticide, hair dyes, organic solvents, etc.

Q: What are the **clinical features of Non-Hodgkin lymphoma (NHL)**?

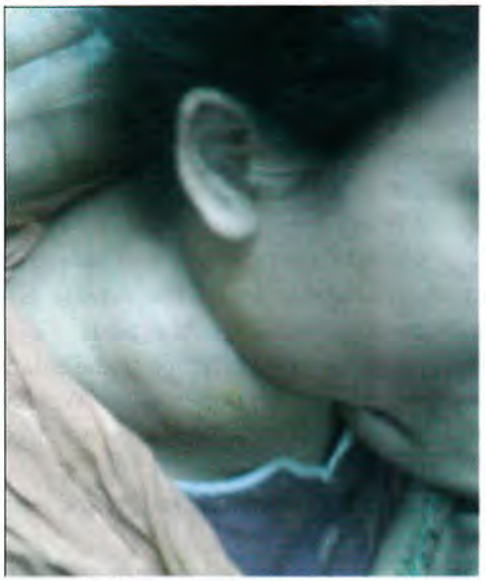
A: As follows:

- NHL can occur at any age; but peak incidence is 65–70 years.
- It is multicentric in origin and spreads rapidly to noncontiguous areas. The disease is usually widespread at the time of diagnosis.
- Discrete, painless, firm, lymph nodal enlargement is the most common presentation. Waldeyer ring and epitrochlear lymph nodes are frequently involved.
- B symptoms of fever, night sweats and weight loss are less prominent.
- Extranodal presentations are more common than Hodgkin disease. May involve gastrointestinal tract (stomach), lung, thyroid, skin, testes and central nervous system (CNS). Skin involvement (T-cell lymphoma) presents as Mycosis fungoides and **Sézary** syndrome. Oropharyngeal involvement occurs rarely. Compression syndrome may occur, such as paraplegia due to compression of spinal cord by an extradural lymphoma, dysphagia, breathlessness, vomiting, intestinal obstruction, ascites and limb oedema, SVC obstruction.
- Bone marrow involvement is more common in low grade (60%) and less in high grade (10%).

- Involvement of liver and spleen results in hepatosplenomegaly.
- Bone involvement may manifest as pathological fractures with pain.



Axillary lymphadenopathy



Cervical lymphadenopathy

Q: What **investigations** are done in NHL?

A: Similar to HL, with the following:

- Routine bone marrow and trephine.
- Immunotyping of surface antigen to distinguish T-cell and B-cell tumours (done on blood, marrow or nodal material). CD 20 should be done.
- Immunoglobulin determination (IgG or IgM paraprotein, which serves as markers for treatment response).
- Uric acid.

Q: What is **Waldeyer ring**?

A: It is a circle of lymphatic tissue in posterior part of oropharynx and nasopharynx, which includes tonsils and adenoids. It is involved in NHL, and rarely in HL.

Q: What are the **treatments** of NHL?

A: As follows:

Low-grade NHL: Not cured by any therapy. No therapy, if the patient is asymptomatic.

Indications of treatment are:

- Marked systemic symptoms.
- Bone marrow failure.
- Features of compression [superior vena caval (SVC) obstruction, spinal cord, gut obstruction and ascites].
- Large lymphadenopathy causing discomfort or disfigurement.

Treatment options include:

- Radiotherapy, for stage I.
- Chemotherapy is needed in most cases. Chlorambucil orally may be used. More aggressive combination therapy may be tried in younger age.
- In monoclonal antibody therapy rituximab (anti-CD 20 antibody) is effective in 60% cases. Synergistic effects are seen with standard chemotherapy.
- Autologous stem cell transplantation can also be given.

High-grade NHL

- Chemotherapy (R-CHOP: rituximab, cyclophosphamide, hydroxydaunorubicin, vincristine and prednisolone).
- Radiotherapy—for stage I and to reduce bulk of the disease.
- Autologous stem cell transplantation for relapse chemosensitive disease.

Q: What is the **prognosis?**

A: As follows:

1. Low-grade lymphoma has a slow indolent course. Median survival up to 10 years. Transformation to high grade is associated with poor prognosis.
2. In high-grade lymphoma, 80% respond to initial therapy, and 35% are disease-free for 5 years.
3. Adverse prognostic factors in NHL includes:
 - Age >60 years.
 - Stage III or IV (advanced disease).
 - High serum LDH level.
 - Performance status ECOG 2 or more.
 - More than one extranodal site of involvement.

4. In case of high-grade NHL, 5-year survival of patient with adverse prognostic factors (high-risk score) is 25%, while that of patients without adverse prognostic factors (low-risk score) is 75%.
5. Relapse is associated with a poor response to further chemotherapy (<10% 5-year survival); but in patients under 65 years, bone marrow transplantation improves survival.

Q: What are the **differences** between HL and NHL?

A: As follows:

Features	Hodgkin lymphoma	Non-Hodgkin lymphoma
Age	Bimodal. First peak at 20–30 years and second peak at 50–70 years	Median age 65–70 years.
LN involvement	Unifocal, usually localized to a single axial group (cervical and mediastinal)	Multicentric, more frequent involvement of peripheral LN
Mesenteric LN and Waldeyer ring	Rarely involved	Commonly involved
Epitrochlear LN	Rarely involved	Commonly involved
LN spread	Orderly spread by contiguity	Noncontiguous spread (via blood)
Extranodal involvement	Less common, occurs late	More common, occurs early
Systemic features or B symptoms	Common	Less common
Alcohol-induced discomfort at lymph node site	Present	Absent
Pel–Ebstein fever	May occur	Does not occur
Pruritus	Common	Less common
Histology	Reed–Sternberg cells (hallmark)	Absent
Bone marrow involvement	Early	Late
Prognosis	High cure rate	Low cure rate (low-grade tumours are incurable)

Generalized Lymphadenopathy (Chronic Lymphatic Leukaemia)

Usual instructions by the examiner:

- Perform the general examination.
- Examine the neck and relevants.

Presentation of a Case (Elderly or Middle Aged)

- Present as described in generalized lymphadenopathy.

Q: How does the patient of CLL usually **present**?

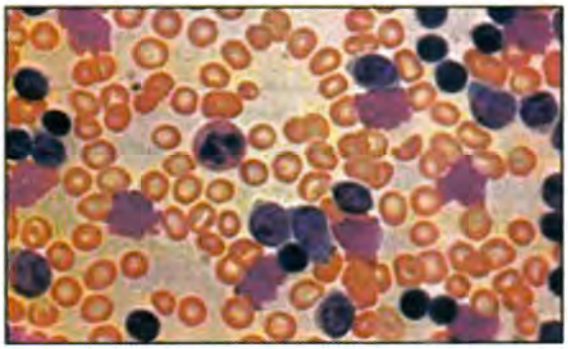
A: Common in the elderly, M:F = 2:1, involving B lymphocyte, after 45 years (usually 60–70 years).

- Asymptomatic, diagnosed incidentally in routine examination.
- General features, such as malaise, weakness, fatigue, weight loss and night sweating.
- Features of anaemia.
- Recurrent infection.
- Generalized lymphadenopathy (detected on routine examination).
- Hepatosplenomegaly (huge splenomegaly, if autoimmune haemolytic anaemia).

Q: What **investigations** do you suggest?

A: As follows:

1. CBC: Hb% (low), leucocytosis (50–200 × 10^9/mm^3), differential count (DC) shows increased lymphocytes.
2. 95%, with mostly small lymphocyte, platelet is normal, low or slightly increased.
3. Bone marrow (increased lymphocytes).
4. Others:
 - Reticulocyte (high in autoimmune haemolytic anaemia).
 - Coombs test (positive in autoimmune haemolytic anaemia).
 - Paraproteins (may be increased).
 - Uric acid (high).
 - Immunophenotyping of B-cell antigen (CD19 and CD23) and T-cell antigen (CD5).



Chronic lymphatic leukaemia

Q: What is **CLL?**

A: It is a neoplastic disorder of lymphocyte that usually involves B-lymphocytes and rarely T-lymphocytes (5%). More in male than in female (2:1); occurs usually after 45 years of age.

Q: What are the **stages** of CLL?

A: There are three stages **(Binet staging)**:

Stage A (60%):

- No anaemia.
- No thrombocytopaenia.
- Less than three areas of LN involvement.

Stage B (30%):

- No anaemia.
- No thrombocytopaenia.
- Three or more areas of LN involvement.

Stage C (10%):

- Anaemia.
- With or without thrombocytopaenia.
- Regardless of area of LN involvement.

N.B. Lymphoid enlargement includes cervical, axillary, inguinal, also liver and spleen.

Another staging **(Rai staging)**:

- **Stage 0:** Lymphocytosis (in blood and bone marrow) >15000/cmm, without lymphadenopathy, hepatosplenomegaly, anaemia or thrombocytopaenia.
- **Stage I:** Lymphocytosis with lymphadenopathy (without hepatosplenomegaly, anaemia or thrombocytopaenia).
- **Stage II:** Lymphocytosis with hepatomegaly or splenomegaly (with or without lymphadenopathy).
- **Stage III:** Lymphocytosis with anaemia (Hb% <11 g/dL) with or without hepatomegaly or splenomegaly.
- **Stage IV:** Lymphocytosis with thrombocytopaenia (<100000/cmm) with or without lymphadenopathy, hepatomegaly, splenomegaly or anaemia.

Q: Why **anaemia** in CLL?

A: Anaemia is due to:

- Bone marrow infiltration.
- Autoimmune haemolytic anaemia.

Q: How to **treat** CLL?

A: Treatment depends on stage of disease:

- **Stage** A: No treatment, unless progression occurs. The patient survives for long time (reassurance and follow-up). Life expectancy is normal in older patients.
- **Stage B:** No treatment, if the patient is asymptomatic.
- **Stage C:** Usually treatment is necessary.

Indications of treatment in CLL:

- Evidence of marrow failure indicated by worsening of anaemia or thrombocytopaenia.
- Massive or progressive lymphadenopathy or splenomegaly.
- Doubling of lymphocyte count in 6 months.
- Symptoms (fever, night sweating and weight loss).
- Presence of haemolysis or other immune-mediated cytopaenias.
- Recurrent infection.

Mode of treatment:

1. Symptomatic:
 - For anaemia and thrombocytopaenia: Prednisolone, blood transfusion should be given. If it is refractory or recurrent, then splenectomy may be done, which is also indicated for hypersplenism.
 - Infection: Antibiotic, immunoglobulin (γ-globulin 0.4 g/kg/month).
 - Local radiotherapy for LN causing discomfort or local obstruction and symptomatic splenomegaly.

2. Specific:
 - Chlorambucil 5 mg daily; adjust the dose according to blood count.
 - Fludarabine alone or with cyclophosphamide or mitoxantrone (with or without steroid) is very helpful. Fludarabine should be avoided in autoimmune haemolytic anaemia as it aggravates anaemia.
 - Combination therapy with rituximab (ineffective alone). Usually rituximab plus fludarabine with or without cyclophosphamide is the treatment of choice.
 - Alemtuzumab may be used in patient that progresses after fludarabine.

- Allogenic stem cell transplantation may be curative, but only used in those patient whose disease cannot be controlled by standard therapies.

Q: What is **Richter syndrome**?

A: When CLL is transformed to aggressive high-grade lymphoma, it is called Richter syndrome. Its prognosis is poor with median survival of less than 1 year.

Q: What is the **prognosis** of CLL?

A: As follows:

- Median survival is about 6 years.
- Stage A may be normal life expectancy.
- In stage C, median survival is 2–3 years.
- About 50% die from infection and 30% from causes unrelated to CLL.
- Rarely, acute blastic crisis may occur.

Purpura

Usual instructions by the examiner:

- Look at the legs. What is your diagnosis? What else do you want to see?

Look at the following points:

1. Whether they blanch on pressure or not (purpura does not blanch).
2. Whether they are palpable and painful or not (palpable painful purpura is of vascular origin and nonpalpable purpura indicates thrombocytopaenia).
3. Colour change (progressive colour change in purpura from red to dark pigmented).
4. Distribution of purpura:
 - Buttock, ankle (Henoch–Schönlein purpura).
 - Extensor surface of forearm, dorsum of hand, leg (senile purpura and drugs).
 - Generalized purpura.

Presentation of a Case

- There is multiple purpura involving both the legs below the knee; some are red and some are dark, and does not blanch on pressure (describe whether palpable or nonpalpable).





Purpura

Q: What do you think are the **causes** in this case?

A: Describe the causes according to age and sex.

In the **elderly**, the causes are:

- Senile purpura (usually on extensor surface of forearm and leg).
- Drug-induced purpura (distribution is like senile purpura) and the usual drugs are steroids, NSAIDs and anticoagulant.
- Leukaemia.
- Aplastic anaemia.
- Scurvy.
- Paraproteinaemia.

In **young** or **child**, the causes are:

- Idiopathic thrombocytopaenic purpura (ITP).
- Henoch–Schönlein purpura (involving buttock and legs).
- Drug induced.
- Acute leukaemia.
- Infections: Viral (dengue) or meningococcal septicaemia.

Q: In a child, there is purpura in the leg. What **else** do you want to see?

A: Purpura in buttock, history of arthritis, abdominal pain, bloody diarrhoea, haematuria (Henoch–Schönlein purpura).

N.B. In any age, mention the causes as follows (if present):

- If Cushingoid facies, due to steroid.
- If patient looks toxic, due to septicaemia.
- If evidence of rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), due to disease itself or due to NSAIDs or steroids.

Q: What **else** do you like to examine to find out the cause?

A: As follows:

- History of fever (dengue), meningococcal septicaemia (patient is toxic) and other infection.
- History of fever, arthritis, bloody diarrhoea, abdominal pain, haematuria (Henoch–Schönlein purpura), history of drugs.
- Blood dyscrasia.
- Anaemia (leukaemia and aplasia).
- Bleeding gum, corkscrew hair and perifollicular haemorrhage (scurvy).
- Any evidence of collagen disease (SLE and RA).
- Other disorders [uraemia, CLD, disseminated intravascular coagulation (DIC) and metabolic disorder].
- Examine the LNs, liver, spleen and bony tenderness (leukaemia).

Q: What are the **differential diagnoses** of purpura?

A: As follows:

- Drug rash.
- Spider angioma or telangiectasia (blanches on pressure, but purpura does not).
- Erythema nodosum (painful and nodular).
- Mosquito bite (usually blanches on pressure, but sometimes may not blanch, if there is extravasation of blood).
- Campbell de Morgan spots (common in elderly): These are small, nodular, reddish lesions that do not blanch on pressure, occur on trunk and upper abdomen, and resolve spontaneously. These are benign angioma, common in middle-aged and the elderly. Malignant change occurs rarely (suggested by itching, rapid increase in size and increased pigmentation).



Campbell de Morgan spot

Q: What **investigations** should be done in purpura?

A: As follows:

1. Hb%, TC, DC, ESR, platelet and PBF.
2. If pancytopaenia or thrombocytopaenia, perform bone marrow study (dry tap in aplastic anaemia, increased megakaryocyte in ITP).
3. Other investigations (according to suspicion of causes):
 - Coagulation screen [bleeding time (BT), clotting time (CT), prothrombin time (PT), activated partial thromboplastin time (APTT) and fibrinogen degeneration products (FDP)] for haemophilia and Christmas disease, and other coagulation factors (DIC).
 - Blood culture (septicaemia).
 - ANA, anti-doublestrand DNA (for SLE).
 - Antiphospholipid antibody.
 - Liver function tests (in CLD).
 - Renal function tests (in CRF).

Q: What is **Hess test**?

A: It is a bedside test, also called tourniquet test. In this test, a sphygmomanometer cuff is inflated over the upper arm between systolic and diastolic blood pressure, kept for 5 minutes and then deflated. Again after 5 minutes, look for petechiae in cubital fossa and near the wrist joint. Normally, there may be <5 petechiae. If >10 petechiae in 2.5 cm^2 area are observed, it indicates thrombocytopaenia. If platelet is <60,000, it is usually positive.

Causes of positive Hess test: It is usually positive in cases of thrombocytopaenia or platelet functional abnormality or increase in capillary fragility. (This test is frequently done to diagnose dengue haemorrhagic fever in which, if number of petechiae is >20, it is definitely positive.)

Read the following topics in relation to purpura:

Q: What is **purpura**? What are the **causes**?

A: It is the spontaneous bleeding or extravasation of blood from the capillary in the skin and mucous membrane that does not blanch on pressure, and there is progressive colour change.

There are **two types** of purpura:

- Small and discrete of pinhead size called petechiae.
- Large and ill-defined called ecchymosis.

Causes of purpura:

- Thrombocytopaenic.
- Vascular.
- Coagulation defect.

***Thrombocytopaenic purpura*:**

1. Primary or ITP.
2. Secondary:
 - Aplastic anaemia (due to any cause).
 - Leukaemia.
 - Secondary deposit in bone marrow.
 - SLE.
 - Others: DIC, CLD and TTP (thrombotic thrombocytopaenic purpura), massive blood transfusion.

***Vascular purpura*:**

1. Congenital (hereditary haemorrhagic telangiectasia, Ehlers–Danlos syndrome).
2. Acquired
 - Senility (elderly patient).
 - Henoch–Schönlein purpura (in children, and rarely in the elderly).
 - Drug-induced (NSAIDs, thiazide, steroid, sulphonamide, penicillin and thiouracil).
 - Infections: SBE, typhoid, meningococcal infection, septicaemia and viral infections (infectious mononucleosis, measles, chicken pox, dengue haemorrhagic fever).
 - Scurvy.
 - Metabolic disorder [chronic renal failure (CRF) and Cushing syndrome].
 - Collagen disease (RA and SLE).
 - Paraproteinaemia (purpura is due to vasculitis or thrombocytopaenia or platelet functional abnormality).
 - Amyloidosis (periorbital).

Coagulation abnormality:

- Haemophilia.
- Christmas disease.
- Anticoagulant therapy.

Q: What are the **causes** of platelet functional abnormality?

A: Platelet functional abnormality (thrombasthenia) occurs in:

- CRF.
- Chronic liver disease (CLD).
- Paraproteinaemia.
- Myeloproliferative diseases.
- Drugs: NSAIDs (aspirin, indomethacin and ibuprofen).

Q: How to **differentiate** in bleeding or purpura, whether due to bleeding abnormality or coagulation abnormality?

A: As follows:

Coagulation abnormality	Bleeding abnormality
Family history usually present	Family history may or may not be present
There is history of prolonged bleeding	No history of prolonged bleeding
Usually there is bleeding into the joint or muscle; purpura is less common or rare	Bleeding into the skin and mucous membrane; purpura is more common
Clotting time is prolonged, but bleeding time and platelet count are normal	Clotting time is normal, but bleeding time is prolonged and platelet count is low
Particular coagulation factor is low or absent, e.g. in haemophilia, factor VIII is absent or low	Coagulation factor is normal, and it is due to either low or defect in platelet function or vascular defect

Idiopathic Thrombocytopaenic Purpura

The usual instructions are:

- Look at the patient. What is your finding?

Presentation of a Case:

(Present as in purpura page 241)

Q: What is **idiopathic thrombocytopenic purpura**?

A: It is a type of thrombocytopenic purpura due to autoantibody against platelet (IgG type). The autoantibody against platelet membrane glycoprotein IIb and IIIa is responsible for premature removal of platelet by monocyte–macrophage system.

Q: What are the **presentations** of ITP?

A: As follows:

- **In child**: Usually acute presentation, previous history of viral infection followed by bleeding or purpura, easy bruising, etc. Chronic ITP is rare in children.
- **In adult:** Common in female, usually insidious onset without preceding viral infection. Presents with purpura, easy bruising, epistaxis or menorrhagia. Features of SLE may be present at presentation or may develop after long time. It may be associated with other autoimmune diseases like thyroid disorder and autoimmune haemolytic anaemia, chronic lymphocytic leukaemia, solid tumour, HIV infection.

On physical examination: Apart from bleeding points, no other physical findings. Splenomegaly is very rare.

N.B. Remember the following points:

- Spontaneous bleeding occurs when the platelet is <20,000/cmm.
- At higher count, there may be bruising, epistaxis and menorrhagia.
- If platelet count is >50,000/cmm, there may not be any features diagnosed on routine test.



Purpura in ITP (legs)



Purpura in ITP (forearm and hands)

Q: **What are the** diseases to be excluded **if ITP is suspected?**

A: As follows:

1. Commonly SLE is to be excluded. In 10% cases, thrombocytopaenia may be the initial manifestation of SLE for many years.
2. Primary antiphospholipid syndrome may present with thrombocytopaenia.
3. Other primary haemorrhagic disorders should be excluded.
4. For this purpose, following investigations should be done:
 - ANA, anti-ds-DNA, antiphospholipid antibody and anticardiolipin antibody.
 - Bone marrow.

N.B. Remember these points:

- In 10% case, ITP may be associated with autoimmune haemolytic anaemia called **Evan syndrome**.
- Patient >65 years old should have bone marrow examination to look for accompanying B-cell malignancy.
- In ITP, low platelet in blood, increased megakaryocyte in bone marrow, prolonged bleeding time and normal clotting time are common.
- HIV testing should be considered, if there is strong suspicion.

Q: How to **investigate ITP?**

A: As follows:

- Full blood count (FBC) (thrombocytopaenia).
- Bone marrow (increased immature megakaryocytes).
- Bleeding time (prolonged).
- Clotting time (normal).
- Antiplatelet antibody (present).
- Antinuclear antibody (ANA) (to exclude SLE).
- Antiphospholipid antibody (positive in 30% cases).

Q: What are the **differences** between ITP in children and adults (or acute and chronic ITP)?

A: As follows:

Features	Child (acute)	Adult (chronic)
Age	Usually 2–6 years	20–30 years
Sex	Any	Predominant in female
Onset	Acute	Chronic
Previous infection	Common	Unusual
Platelet count	<20,000/mm^3	>20,000/mm^3

Features	Child (acute)	Adult (chronic)
Spontaneous remission	Common	Less, <20%
Duration	2–4 weeks	Chronic, months to years

Q: How to treat ITP?

A: Treatment is as follows:

1. **In child:** Usually self-limiting; does not require treatment in most cases. If there is no improvement.
 - Prednisolone (2 mg/kg) should be given if moderate-to-severe thrombocytopaenia (<10,000) and bruising, epistaxis or other bleeding.
 - If still persistent bleeding, IV immunoglobulin (IgG) should be given.
 - In some case, platelet transfusion may be required when there is persistent bleeding [epistaxis, gastrointestinal tract (GIT) bleeding, retinal haemorrhage, intracranial bleeding].
2. **In adult:** Persistent thrombocytopaenia is common. Most patients with platelet count >30 × 10^9/L are stable and do not require treatment unless they are about to undergo a surgery.
 - *First-line therapy:*
 - If spontaneous bleeding, prednisolone 1 mg/kg to be given for 4–6 weeks and then tapered. 66% will respond, but relapse is common when the steroid dose is reduced or stopped. 10–20% usually have long-term remission. If relapse, steroid should be started again.
 - IV immunoglobulin may be given mainly if there is severe haemostatic failure or slow response to steroid alone or surgery is required. Dose of immunoglobulin is 1 g/kg for 3–5 days. Its effect is temporary, persists for 3–4 weeks and is quite expensive. Steroid may be added with immunoglobulin.
 - *Second-line therapy:*
 - If there is frequent relapse (usually two relapses), in primary refractory disease or require high dose of steroid to maintain safe platelet level, splenectomy should be done. There is complete remission in 70% cases and improvement in 20–25% cases. 5–10% require further medical therapy.
 - *Third-line therapy:*
 - If there is failure after splenectomy, other therapy should be considered—corticosteroid, IV immunoglobulin, anti-D infusion, danazol, immunosuppressive therapy (azathioprine, cyclophosphamide, dapsone, vincristine, vinblastine, ciclosporine, mycophenolate mofetil). Also monoclonal antibody like rituximab as well as recombinant thrombopoietin may be given.
 - ***Platelet transfusion*** is not usually used. However, it is used only if persistent or potentially life-threatening bleeding or where emergency splenectomy is done.

N.B. Remember the following points:

- In nonresponder after splenectomy, think of presence of accessory spleen (confirm by radionuclide scan).
- After splenectomy, there is more chance of infection by pneumococcus, meningococcus and *Haemophilus influenzae* (vaccination against these is essential).

Henoch–Schönlein Purpura

Usual instructions by the examiner:

- Look at the patient. What is your finding? What may be the cause?

Presentation of a Case:

(Present as in purpura page 241)

Q: What is the likely **diagnosis**?

A: If the patient is child, may be ITP or Henoch–Schönlein purpura (HSP).

Q: What **else** do you want to see?

A: Buttock. In Henoch–Schönlein purpura, commonly buttock is involved.

Q: What are the **differential diagnoses?**

A: As follows:

- Drug rash.
- ITP.
- SLE.
- Septicaemia.
- Thrombotic thrombocytopenic purpura (TTP).

Q: What **history** do you like to take in Henoch–Schönlein purpura?

A: Arthritis, abdominal pain, bloody diarrhoea and urinary complaint (haematuria).

Q: What is **Henoch–Schönlein purpura** (anaphylactoid purpura)?

A: It is a small vessel vasculitis characterized by purpura or petechial rash, polyarthritis (in big joints), abdominal pain and glomerulonephritis. It is due to circulating IgA-containing immune complex. Follow for 1–3 weeks after upper respiratory tract infection (usually viral). Other factors responsible include food, drugs or vaccination.

Q: What are the **clinical features** of HSP?

A: HSP is more common in boys of 5–15 years of age, but may occur at any age. The common features are:

- Skin lesion: Purpura is common in legs and buttock; face and trunk are spared. May resolves in 2–4 weeks and fresh crops may appear. Angio-oedema occurs in 50% cases.
- Polyarthritis occurs in 70%, commonly involves knee and ankle, may be fleeting type.
- Abdominal pain, colicky in nature, associated with nausea, vomiting, bloody diarrhoea, intussusception and perforation. There is vasculitis; bowel is oedematous and inflamed causing bleeding and obstruction. This may be confused with acute surgical condition.
- Renal disease occurs in 30–70% cases; present with haematuria and proteinuria. It is usually mild. Focal necrotising glomerulonephritis, rarely renal failure may occur. In adults, 25% cases develop severe crescentic or rapidly progressing glomerulonephritis and renal failure (which are less in children).



Arthritis in Henoch–Schönlein purpura



Henoch–Schönlein purpura (buttock)

Q: What **investigations** should be done in HSP?

A: As follows:

- FBC and platelet (nonthrombocytopaenic purpura).
- Urine (proteinuria and haematuria).
- Serum IgA is high in 50% cases (IgA-containing immune complex is also high).
- Skin biopsy from normal and involved skin (it will show leucocytoclastic vasculitis with deposition of IgA and complement C3 in blood vessels).
- Kidney biopsy.

Q: Suggest two **investigations** that are helpful for **diagnosis**.

A: As follows:

- Serum IgA is high in 50% cases (IgA-containing immune complex is also high).
- Skin biopsy from normal and involved skin (vasculitis with deposition of IgA and complement C3 in blood vessels).

Q: Suggest one **investigation** that is helpful for prognosis.

A: **Renal biopsy**: It shows focal and segmental proliferative glomerulonephritis, sometimes with mesangial hypercellularity. In more severe cases, epithelial crescents may be present developing rapidly progressing glomerulonephritis and renal failure. This is less in children. There is IgA deposition within and around blood vessels, glomerular mesangium (it may be confused with IgA nephropathy).

Prognosis of HSP is related to the severity of renal involvement.

Q: How to **treat?**

A: As follows:

- Self-limiting, spontaneous cure in majority of cases.
- Steroid is indicated, if there is GIT and joint symptoms (does not affect the course and

progression of disease). Abdominal pain may be improved in 24 h.
- In renal involvement pulse IV steroid and cytotoxic drugs should be given.
- Recurrence may occur. If so, dapsone may help in cutaneous recurrence.

Q: What is the **prognosis**?
A: Good in children, relatively bad in adults. Adverse factors in adults include hypertension, abnormal renal function and proteinuria >1.5 g/day. But only 1% of patients develop end-stage renal failure.

N.B. Henoch–Schönlein purpura in adults:
- Skin involvement is common (70%).
- Gut and joint involvement occurs in 20% cases.
- Renal involvement is more common than children.
- Myocardial involvement may occur rarely.
- Prognosis is worse in adults than children.

In children:
- Gastrointestinal vasculitis is more common.
- Renal and skin involvement is less common.
- Prognosis is better.

Splenomegaly (Hereditary Haemolytic Anaemia)

Usual instructions:
- Examine the abdomen and relevant.
- Palpate the abdomen. What are your findings (splenomegaly)? What relevant do you like to see?

Presentation of a Case

(The patient is usually of young or early age.)
- Spleen is hugely enlarged, ... cm from costal margin in anterior axillary line towards right iliac fossa.

Q: What are the **causes of splenomegaly** in this young patient?
A: As follows:
- Malaria.
- Kala-azar.
- Hereditary haemolytic anaemia.
- Lymphoma.
- CLD with portal hypertension (causes are Wilson disease and α_1-antitrypsin deficiency).



β-Thalassaemia major

Q: What hereditary haemolytic anaemia this can be?
A: β-Thalassaemia major, HbE disease, β-thalassaemia HbE disease (double heterozygous) and hereditary spherocytosis.

Q: What **relevant** physical findings will you see in hereditary haemolytic anaemia?
A: As follows:
- Anaemia and jaundice.
- Frontal and parietal bossing and mongoloid facies with prominent malar bones.
- Short stature and retardation of growth.
- Also, family history should be taken.

Q: What are the features of **haemolytic anaemia?**
A: **The triad** features of haemolytic anaemia are:
- Anaemia.
- Jaundice.
- Splenomegaly.

Q: How will you **confirm** your diagnosis?
A: Using haemoglobin electrophoresis.

Q: Mention one **simple investigation** that will help your diagnosis.
A: Peripheral blood film (PBF) that shows microcytic hypochromic anaemia.

Q: Mention **another investigation** helpful for your diagnosis.
A: Reticulocyte count (by supravital stain)—high.

Q: What **investigations** do you suggest?
A: As follows:
1. Hb%, TC, DC, ESR and PBF (microcytic hypochromic blood picture).
2. Reticulocyte count (by supravital stain)—high.
3. Haemoglobin electrophoresis.

4. Others:
 - X-ray of skull, hand and other skeletal survey.
 - Serum bilirubin: High (also urinary urobilinogen is high).
 - Serum iron profile: Ferritin (may be high, if haemosiderosis), iron, TIBC.



X-ray skull of β-thalassaemia major

Causes of the microcytic hypochromic blood picture

- Iron-deficiency anaemia (the commonest cause).
- β-Thalassaemia (major and minor).
- Sideroblastic anaemia.
- Anaemia of chronic disease.

Q: What are the **findings** in β-thalassaemia in Hb-electrophoresis?

A: As follows:
- β-Thalassaemia major: Hb-F is more and Hb-A is less.
- β-Thalassaemia minor: Hb-A2 is more.

Q: What are the **radiological findings** in skull in β-thalassaemia major?

A: As follows:
- Widening of diploic space.
- Thinning of outer table.
- Thickening and coarsening of trabeculae, giving rise to hair-on-end appearance.

Read the following in relation to thalassaemia:

Q: What is **thalassaemia?**

A: It is an inherited disorder in which there is impairment of haemoglobin production due to partial or complete failure to synthesize the specific type of globin chain. It is of two types:

1. β-Thalassaemia: In this case, there is an inadequate production of β-chain, causing less production of HbA. It is of two types:
 - β-Thalassaemia major: HbA is less, HbF is more.
 - β-Thalassaemia minor: HbA2 is increased.
2. α-Thalassaemia: In this case, there is an inadequate production of α-chain, therefore less HbA, HbF and HbA2 as all of them contain α-chain.
3. Thalassaemia intermedia, characterized by the combination of homozygous mild β-thalassaemia plus α-thalassaemia. It is usually less severe and does not require blood transfusion as anaemia is mild-to-moderate.

Q: How to **treat** β-thalassaemia major?

A: As follows:
1. Correction of anaemia: Blood transfusion to keep Hb% above 10 g% every 4 months (lifespan of RBC is 4 months).
2. Folic acid 5 mg daily, to be continued.
3. Iron-containing drugs and diet are avoided (iron can only be given if there is deficiency).
4. Repeated blood transfusion may cause haemosiderosis, which can be prevented by chelating agent, desferrioxamine subcutaneously with infusion pump overnight. Ascorbic acid 200 mg daily may be added (it causes urinary excretion of iron). Oral iron-chelating agents such as deferiprone or deferasirox may be used.
 - Others treatment: Injection erythropoietin. It stimulates the bone marrow, increases normal haemoglobin to some extent.
 - Hydroxyurea 1–2 g daily may be helpful (it prevents ineffective erythropoiesis).
5. Specific therapy: Allogenic bone marrow transplantation from HLA-compatible sibling. Also, gene therapy.
6. Splenectomy.
7. Genetic counseling should be offered. It is necessary for prenatal diagnosis that is available.

Indication of splenectomy:
- Huge splenomegaly with pressure symptoms.
- Hypersplenism: As suggested by repeated transfusion in a short interval. FBC shows pancytopaenia.

N.B. Patient with mild thalassaemia (β-thalassaemia minor or α-thalassaemia trait) requires no treatment. Only avoid iron therapy.

Q: What are the **complications** of repeated blood transfusion?

A: As follows:

- Repeated transfusion may cause haemosiderosis (usually when more than 30–50 L of blood is transfused).
- Infections such as hepatitis B, C, D and HIV.

Q: How haemosiderosis can be **prevented**?

A: Haemosiderosis can be prevented by using chelating agent desferrioxamine (1.5–2 g with each unit of blood). It is usually given subcutaneously in the anterior abdominal wall with infusion pump for 12 h. It may also be given with infusion drip (normal saline or aqua). Oral chelating agent such as deferiprone, 75 mg/kg in two-to-four divided doses, is also available. Other oral chelating agent includes deferasirox. Vitamin C, 200 mg daily orally also helps in iron excretion.

Q: If the patient develops severe **abdominal pain**, what is the likely cause?

A: Cholelithiasis (usually pigment stone, due to haemolysis). There may also be splenic infarction. Acute pancreatitis may also occur.

Q: When does **anaemia** develops in a patient with thalassaemia major after delivery?

A: Anaemia develops at the age of 4–6 months. In a normal person, HbF disappears 4–6 months after birth. In adults, HbF is <1%. But in thalassaemia major, HbF is increased.

Q: How can it be **diagnosed before birth**?

A: Prenatal diagnosis is possible by obtaining chorionic villus material for DNA. It should be done if both parents suffer from β-thalassaemia minor. If β-thalassaemia is found in the fetus, then termination of pregnancy is indicated.

Q: What are the presentations of **thalassaemia minor**? What is the **differential diagnosis**?

A: As follows:

- May be asymptomatic.
- There may be features of anaemia (microcytic hypochromic).
- Incidentally during blood count, microcytic hypochromic blood picture.
- Haemoglobin electrophoresis shows high A2.

Thalassaemia minor confuses with iron-deficiency anaemia. However, anaemia is more marked in iron deficiency and relatively less in thalassaemia minor. Also, in iron deficiency, there is low iron, low ferritin and high total iron-binding capacity.

Splenomegaly (Chronic Myeloid Leukaemia)

Usual instructions are:

- Examine the abdomen.
- Palpate the abdomen.

Presentation of a Case

(Patient is usually middle-aged or above 40 years.)

- Spleen is hugely enlarged, ... cm from costal margin in anterior axillary line towards right iliac fossa.

Q: What are the **causes of splenomegaly** in this middle-aged patient?

A: As follows:

- Malaria.
- Kala-azar.
- Chronic myeloid leukaemia (CML).
- Lymphoma.
- CLD with portal hypertension
- Myelofibrosis (if the patient is elderly).
- Tropical splenomegaly syndrome.

Q: What is the **CML**?

A: It is a myeloproliferative disorder characterized by overproduction of myeloid cells and presence of Philadelphia chromosome. It is common in 40–60 years, and peak is 55 years.

Q: What are the **myeloproliferative disorder**?

A: There are four diseases:

- Chronic myelocytic leukaemia.
- Myelofibrosis.
- Polycythaemia rubra vera.
- Essential thrombocythaemia.

These disorders are grouped together because the disease may evolve from one form to another. All myeloproliferative disorders may progress to acute myeloid leukaemia.

Q: What is the common **age** for CML?

A: Usually 30–80 years, and peak is 55 years.

Q: How does the patient usually **present**?

A: As follows:

- May be asymptomatic (25%).
- Splenomegaly (90%, may be huge in 10%). Patient may complain of mass or discomfort, or heaviness or pain in left hypochondrium.
- Unexplained anaemia.
- General features of weakness, malaise, loss of weight and night sweating.

- Repeated infection.
- Bleeding (due to thrombocytopaenia).
- Hepatomegaly (in 50% cases).

Q: Mention **one investigation** that will help in diagnosis or exclude other diagnosis.

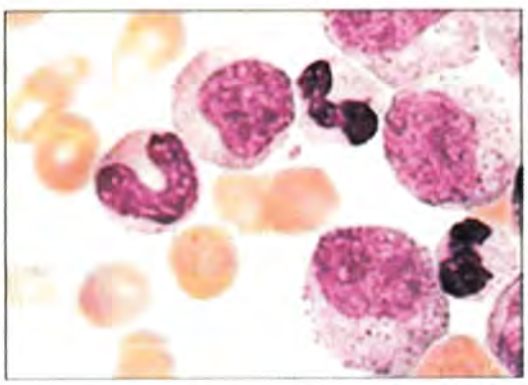
A: FBC with PBF. It will help:

- To diagnose CML.
- Myelofibrosis (it will show leukoerythroblastic blood picture with tear- or pear-drop poikilocytes).
- Pancytopaenia (due to hypersplenism).
- To diagnose malaria.
- To diagnose kala-azar: It shows leucopenia with high lymphocyte and monocyte; repeated blood count shows progressive leucopenia.

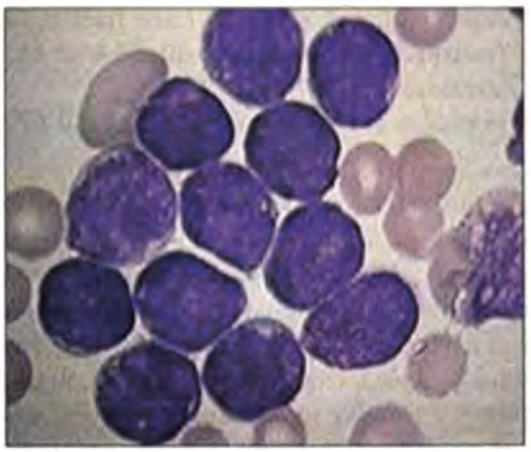
Q: What **investigations** do you suggest?

A: As follows:

1. FBC:
 - Leucocytosis (may be very high).
 - Differential count (DC) shows increase in myelocyte, promyelocyte. metamyelocyte, myeloblast , 10% increase in neutrophil and also basophil and eosinophil.
 - Platelets are increased.
 - Nucleated red cells are common.
2. Bone marrow study (hypercellular marrow with increased myeloid precursors). Cytogenetic analysis for Philadelphia chromosome; also RNA analysis to see the presence of BCR–ABL gene product.
3. Other tests:
 - Philadelphia chromosome (positive in 95% cases).
 - LAP score (decreases).
 - Serum uric acid (increases).
 - Serum vitamin B_{12} (increases).
 - Serum LDH (increases).



Chronic myeloid leukaemia (myelocytes and promyelocytes are seen)



Chronic myeloid leukaemia in blastic transformation (myeloblasts are seen)

Q: What are the **clinical phases** or **types** of CML?

A: There are three phases:

- Chronic phase.
- Accelerated phase.
- Blastic crisis.

Q: What are the **causes of death** in CML?

A: As follows:

- Blastic crisis.
- Secondary infection.
- Myelofibrosis.

Q: What is **blastic** crisis? How can you **suspect** blastic crisis **clinically?**

A: It means the disease is transformed to acute leukaemia. It may be myeloid (70%) or lymphatic type (30%); and it occurs at a rate of 10%/year, relatively refractory to treatment and is the cause of death in majority of cases. Prognosis is poor in myeloid type. Blastic crisis in CML can be suspected, if:

- Rapid deterioration of the patient.
- Increasing splenomegaly.
- Blood picture shows increase in number of blast cells and increasing basophil.

Q: How to **treat** CML?

A: Treatment depends on the phase of the disease such as chronic phase, and accelerated or blastic crisis.

1. **Treatment of chronic phase:**
 - Imatinib is the first-line therapy. It shows 76% (95% in some cases) response with disappearance of Philadelphia chromosome after 18 months. It is a tyrosine kinase inhibitor that acts by blocking the enzymatic action of BCR–ABL fusion protein. It reduces uncontrolled proliferation of white blood

cells (WBC). Dose is 400 mg daily. In some cases, 600–800 mg may be given to overcome the resistance. It can be continued indefinitely.

- If failure to respond to imatinib, second-generation tyrosine kinase inhibitor such as dasatinib or nilotinib or allogenic bone marrow transplantation should be considered.
- Alternately, hydroxyurea or α-interferon that were previously used for initial control are still useful. However, hydroxyurea does not diminish Philadelphia chromosome or affect blastic crisis. α-Interferon was given alone or with the chemotherapeutic agent Ara-C. It controls CML in chronic phase in about 70% of patients and causes disappearance of Philadelphia chromosome in 20% cases. It was a first-line drug before imatinib.
- Busulphan is used previously. Not used now-a-days.
- Bone marrow transplantation (BMT) from allogenic-matched sibling donor (usually below the age of 40 years and in early chronic phase); 70% cure.

2. **Treatment of accelerated phase and blastic crisis:**
 - Treatment is difficult; imatinib is indicated if the patient has not received it.
 - Hydroxyurea (hydroxycarbamide) can be effective.
 - Low-dose cytarabine can be given.

N.B. Remember the following points regarding chemotherapeutic drugs that were previously used:

- Both busulphan and hydroxyurea: Of lessor no use now.
- Busulphan controls leucocyte quickly, but there is greater risk of marrow depression and rarely interstitial fibrosis of lung (**Busulphan lung**). It also causes increased pigmentation.
- Hydroxyurea is preferred than busulphan; but controls leucocyte countless quickly than busulphan; and bone marrow depression is also less.
- None of these drugs affect the onset of blast transformation or diminishes Philadelphia chromosome and little effect on survival.
- Bone marrow transplantation is indicated in whom the disease is not well controlled, in whom the disease progress after initial control or for those who have accelerated phase disease.

Q: What are the therapies that may **cure** CML?

A: Bone marrow transplantation (BMT), imatinib and α-interferon.

Q: What is the **prognosis** of CML?

A: As follows:

- With imatinib therapy, complete haematological remission in up to 95% cases; and 70–80% of these have no detectable BCR–ABL transcript. Event-free and overall survival appears to be better.
- Following stem cell transplantation, there is 70% cure in chronic phase in young patients.
- Without treatment the median survival is 3–4 years; some may survive up to 10 years.
- If there is blastic crisis, prognosis is poor. Median survival is 6 months.
- CML may transform to myelofibrosis.

Splenomegaly (Myelofibrosis)

Usual instructions are:

- Examine the abdomen.
- Palpate the abdomen.

Presentation of a Case

(The patient is usually middle-aged or elderly.)

- Spleen is hugely enlarged, ... cm from costal margin in anterior axillary line towards right iliac fossa.

Q: What are the **causes of splenomegaly** in this middle-aged patient?

A: As follows:

- Malaria.
- Kala-azar.
- Myelofibrosis.
- CML.
- Lymphoma.
- CLD with portal hypertension

Q: What is **myelofibrosis** and how does the patient usually **present**?

A: Myelofibrosis is a disorder of unknown cause characterized by bone marrow fibrosis, extramedullary haemopoiesis and leucoerythroblastic blood picture. There is clonal proliferation of the stem cells. Fibrosis in the marrow is due to hyperplasia of abnormal megakaryocyte, which releases fibroblast stimulating factors.

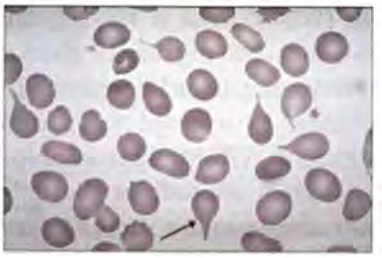
It is common above 50 years. History of polycythaemia rubra vera is found in 25% cases; and 50% have *JAK*-2 mutation seen in polycythaemia rubra vera (PRV). Features are:

- May be asymptomatic. Mass in the left hypochondrium or hepatosplenomegaly.
- General features of malaise, weakness, loss of weight, night sweat, repeated infection and bleeding.
- There may be peptic ulcer, pruritus after hot bath and gout.

Q: What **investigations** do you suggest?

A: As follows:

1. FBC and PBF examination
 - Leucocytosis, leucoerythroblastic blood picture (immature nucleated RBC) and premature cells of WBC series (myelocytes and myeloblast).
 - PBF shows tear-drop RBCs (tear-drop poikilocytes).
 - Platelets are very high, and later on decreased. Giant forms may be seen.
 - Anaemia is usually macrocytic, and pancytopaenia may occur.
2. Bone marrow may be dry tap; trephine biopsy should be done (which shows increased megakaryocyte, increased reticulin and fibrous tissue).
3. Others: leucocyte alkaline phosphatase (LAP) score is increased, uric acid is high and folic acid is low; genetic test may show *JAK*-2 mutation.



Tear-drop poikilocyte in myelofibrosis

Q: How to **treat** of myelofibrosis?

A: As follows:

- Correction of anaemia by blood transfusion and folic acid.
- Hydroxyurea (it reduces WBC and splenomegaly).
- Radiotherapy for huge spleen.
- Splenectomy, if huge spleen with pressure symptoms and hypersplenism.
- Bone marrow transplantation (if the patient is young).
- A new drug called ruxolitinib (inhibitor of JAK-1 and JAK-2) may be used in some patients.

Prognosis: Median survival is 4 years (ranges from 1 to 20 years).

Q: What are the **causes of death** in myelofibrosis?

A: As follows:

- Transformation to AML (10–20%).
- Infection.
- Bleeding (from GIT).
- Cardiovascular problem.

Q: How to **differentiate myelofibrosis** from CML?

A: As follows:

- Marrow finding.
- Philadelphia chromosome (absent in myelofibrosis).
- LAP score (increases in myelofibrosis and decreases in CML).
- In CML, WBC count is very high with precursors of granulocytes, which are absent in myelofibrosis.

Iron-deficiency Anaemia

Usual instructions by the examiner:

- Perform the general examination.

Presentation of a Case

- The patient is pale, moderately anaemic.

My diagnosis is anaemia.

Q: What is the **commonest** anaemia?

A: Iron-deficiency anaemia.

Q: What **simple investigation** is done to diagnose iron-deficiency anaemia?

A: Peripheral blood film (PBF) (microcytic, hypochromic blood picture).

Q: What **history** would you take in iron-deficiency anaemia?

A: As follows:

- Bleeding from any site (haemorrhoid, haematemesis, melaena, gum bleeding, any bleeding disorder, injury).
- In female (menorrhagia and repeated pregnancy).
- Drugs (NSAID in patient with arthritis).
- History of malabsorption.
- Less intake of food (anorexia, dysphagia and poverty).
- Chronic illness (e.g. malignancy).

Q: Tell **one peculiar symptom** in iron-deficiency anaemia.

A: Pica—it means eating of unusual items such as earth, coal, ice or some foods in excess like tomato, sour foods. The cause is unknown.

Causes of iron-deficiency anaemia:

- Bleeding due to any cause: The commonest from gastrointestinal tract (GIT) (haemorrhoid, colorectal carcinoma, Ca-stomach, diverticulitis, angiodysplasia), menorrhagia in female.
- Hookworm (also schistosomiasis).
- Less intake of food.
- Malabsorption.
- More demand (pregnancy).

Q: What **investigations** are done in iron-deficiency anaemia?

A: As follows:

1. Test to confirm iron-deficiency anaemia
 - Full blood count with PBF (microcytic hypochromic blood picture).
 - Serum iron, TIBC and ferritin (low iron, increased TIBC and low ferritin).
2. Test to find out the causes
 - Stool for ova or cyst of hookworm, and occult blood test.
 - Upper gastrointestinal (GI) tract endoscopy (oesophageal varices, peptic ulcer and carcinoma stomach).
 - Proctoscopy (haemorrhoid), sigmoidoscopy or colonoscopy (neoplasm, polyp, diverticulum, ulcer, angiodysplasia of colon).
 - USG of abdomen (any mass, fibroid uterus).
3. Bone marrow to see stainable iron (by Prussian blue shows empty stain); **not a routine**, may be done in some cases.

Causes of microcytic hypochromic blood picture

- Iron-deficiency anaemia (the commonest).
- Thalassaemia.
- Sideroblastic anaemia.
- Anaemia of chronic disorder.

Q: What is the **daily requirement** of iron?

A: Daily requirement of iron is 1.0 mg/day. But in pregnancy, extra 2.5 mg/day is needed (hence total 3.5 mg/day is required).

Q: How to **treat** iron-deficiency anaemia? How **long** will you continue the treatment?

A: If there is severe anaemia or haemoglobin is low, anaemia should be corrected by blood transfusion. Iron therapy: Oral ferrous sulphate (200 mg 8 hourly), ferrous gluconate (300 mg 12 hourly) or ferrous fumarate. To be given for 3–6 months after heamoglobin is normal to replenish the iron store. Delayed-release preparation of iron is not helpful, as they release iron beyond the upper small intestine, where it cannot be absorbed. If the patient is unable to take orally, sorbitol 1.5 mg/kg injection intramuscularly (IM) may be given daily. It can cause skin pigmentation. Treatment of cause should be done (e.g. menorrhagia, haemorrhoid, etc.).

Q: How to see the **response** to iron therapy?

A: Increase in reticulocytes after 1 week.

Related Questions–Answers about Anaemia

Q: Classify anaemia.

A: Anaemia may be classified in two ways: Aetiological (based on cause) and morphological (based on morphology of RBC).

Aetiological:

1. **Haemorrhagic anaemia (due to blood loss):**
 - Acute: Trauma, postpartum bleeding, haematemesis, melaena, epistaxis.
 - Chronic: Hook worms, haemorrhoids, excessive menstrual loss, bleeding peptic ulcer, etc.
2. **Dyshaemopoietic anaemia (due to inadequate production of RBC):**
 - Deficiency anaemia: Iron, vitamin B_{12}, folate deficiency.
 - Aplastic anaemia (bone marrow failure, which may be primary or secondary to some other diseases or drugs).

- Anaemia of chronic disorder (ACD): SLE, rheumatoid arthritis, CRF.
- Others: Hypothyroidism, sideroblastic anaemia, malignancy.

3. **Haemolytic anaemia:**
 - Genetic: Red-cell-membrane defect (e.g. hereditary spherocytosis, eliptocytosis, stomatocytosis), haemoglobin abnormality (thalassaemia, sickle-cell anaemia) or enzyme defects (glucose-6-phosphate dehydrogenase deficiency, pyruvate kinase deficiency).
 - Acquired: Autoimmune, toxic, mechanical and infectious causes.

Morphological (depending on mean corpuscular volume (MCV) and **mean corpuscular haemoglobin concentration** (MCHC):

1. Normocytic normochromic anaemia (normal MCV and MCHC).
2. Microcytic hypochromic anaemia (low MCV <76 fl, low MCHC <30 g/dL).
3. Macrocytic anaemia (high MCV >96 fl).
4. Dimorphic anaemia (two-cell lines: Macrocytes and microcytes).

Q: What are the causes of **normocytic normochromic anaemia**?

A: As follows:

- Anaemia of chronic disorder.
- Chronic infection (e.g. tuberculosis).
- Collagen disease (e.g. SLE, RA).
- Malignancy.
- Endocrine disease.
- Sideroblastic anaemia.

Q: What are the causes of **microcytic hypochromic anaemia**?

A: (See above).

Q: What are the causes of **macrocytic anaemia**?

A: As follows:

1. **Macrocytosis with megaloblastic marrow are found in:**
 - Vitamin B_{12} deficiency.
 - Folic acid deficiency.
2. **Macrocytosis with normoblastic marrow are found in:**
 - Chronic liver disease.
 - Chronic alcoholism.
 - Hypothyroidism.
 - Haemorrhage.
 - Haemolysis.
 - Others: Sideroblastic anaemia, pure red cell aplasia, azathioprine therapy.

Q: What is **dimorphic anaemia**? What are the **causes**?

A: When both microcytes and macrocytes are found, this is called dimorphic anaemia. Causes are:

- Combined iron, B_{12} and folate deficiency.
- Sideroblastic anaemia.
- Treatment of anaemia.

Q: What are the causes or mechanisms of **anaemia of chronic disorder**?

A: Actual mechanism is unknown. It is due to abnormality of iron metabolism and erythropoiesis. There is less erythropoietin. Also, red cell survival is short.

Q: What are the **signs** that may point to a specific cause of anaemia?

A: As follows:

Sign	Cause of anaemia
Triad of anaemia, jaundice and splenomegaly	Haemolytic anaemia
Angular cheilitis, glossitis, koilonychia	Iron-deficiency anaemia
Glossitis	Iron-deficiency anaemia, vitamin B_{12} deficiency, folate deficiency
Splenomegaly	Malaria, chronic haemolytic anaemia, acute infection, leukaemia, lymphoma, portal hypertension
Neurological changes (dementia, optic atrophy and features of subacute combined degeneration of spinal cord) **and lemon-yellow tint.**	Vitamin B_{12} deficiency (megaloblastic anaemia).
Bony change (frontal and parietal bossing)	Hereditary haemolytic anaemia
Leg ulcer	Sickle-cell anaemia, paroxysmal nocturnal haemoglobinuria (PNH)
Bony tenderness	Acute leukaemia, multiple myeloma, lymphoma, myelofibrosis

Q: What is **spurious anaemia**?

A: When plasma volume is increased and haemoglobin is relatively low, it is called spurious anaemia. It is found in pregnancy.

Q: What is **spurious polycythaemia**?

A: Here haemoglobin is relatively increased due to low plasma volume. This is found in dehydration.

Q: How to **investigate** a patient with anaemia?

A: Detailed history, physical examination and finally relevant laboratory investigations are done to investigate a patient with anaemia.

History of the patient:

- Dietary history (to diagnose deficiency anaemia such as iron, vitamin B_{12} and folic acid deficiency).
- Malabsorption.
- Any history of bleeding (haemorrhoid, epistaxis, haematemesis, melaena, menorrhagia in female, etc).
- In female: Multiple pregnancies, repeated abortion.
- Drug history: NSAIDs, steroid, drugs causing bone marrow suppression (e.g. cytotoxic drugs); drugs causing haemolysis (e.g. sulfasalazine, methyldopa, etc.).
- History of surgery: Gastrectomy or partial gastrectomy, ileal surgery (responsible for vitamin B_{12} absorption).
- Family history (in case of hereditary haemolytic anaemia).
- History of any chronic disease (e.g. SLE, CRF, etc).

Clinical examination: See page 254.

Laboratory investigations:

1. Full blood count (Hb%, TC, DC, ESR, platelet count):
 - Pancytopaenia: May be due to aplastic anaemia, hypersplenism, megaloblastic anaemia, aleukaemic leukaemia.
2. PBF examination: Following findings may be found that indicate particular causes of anaemia (see in the table on the right).
3. Reticulocyte count: High in haemolytic anaemia.
4. MCV and MCHC.
5. Bone marrow examination: Megaloblastic anaemia, aplastic anaemia, bone marrow infiltration (secondary deposit), ring sideroblasts (in sideroblastic anaemia).
6. Other investigations according to suspicion of cause.

Further investigation of microcytic hypochromic anaemia (low MCV and low MCHC):

- For iron-deficiency anaemia: Serum iron, TIBC, serum ferritin.
- For hereditary haemolytic anaemia: Haemoglobin electrophoresis, skeletal survey.
- For sideroblastic anaemia: According to history, bone marrow examination (ring sideroblasts)
- For anaemia of chronic disease: According to history of the patient.

Further investigations for macrocytic anaemia (high MCV):

- Bone marrow is done. If megaloblast seen, serum B_{12} and folic acid assay should be done. If normoblast is found, further investigation should be done according to history (see above).

Q: What diseases may be **diagnosed from PBF?**

A: As follows:

Finding	Description	Common diagnoses
Anisocytosis	Variation in size of RBC	Iron-deficiency anaemia, megaloblastic anaemia, sideroblastic anaemia
Poikilocytosis	Variation in shape of RBC	Iron-deficiency anaemia, thalassaemia, sideroblastic anaemia
Microcytosis	MCV <76 fL	Iron-deficiency anaemia, thalassaemia, sideroblastic anaemia, anaemia of chronic disorder
Macrocytosis	MCV >100 fL	Vitamin B_{12} and folic acid deficiency, chronic liver disease, alcohol, hypothyroidism, zidovudine
Hypochromia	Central pallor of RBC is increased in size (lower haemoglobin content)	Iron-deficiency anaemia, thalassaemia, sideroblastic anaemia, anaemia of chronic disorder
Basophilic stippling or punctate basophilia	Deep-blue dots scattered in cytoplasm of RBC (seen with Romanowsky staining)	Chronic lead poisoning, dyshaemopoiesis
Target cells	Flat red cells with a central mass of haemoglobin (dense area) surrounded by a ring of pallor (pale area) and an outer ring of haemoglobin (dense area)	Iron-deficiency anaemia, thalassaemia, haemoglobin C disease, CLD, splenectomy
Howell–Jolly bodies	Small, round remnants of nuclear material in RBC. These are normally removed by spleen.	Hyposplenism, postsplenectomy, dyshaemopoiesis

Heinz bodies (Ehrlich bodies)	Formed from denatured, aggregated haemoglobin in RBCs (seen with supravital staining with brilliant cresyl blue).	Thalassaemia, haemolysis in glucose-6-phosphate dehydrogenase deficiency, asplenia and CLD, drug-like sulfasalazine, dapsone
Acanthocytes (spur cells)	RBC with irregular spicules	Abetalipoproteinaemia
Burr cells	RBC with regularly placed spicules	CRF
Schistocytes	Fragmented RBC. These are found in microangiopathic haemolytic anaemia.	Causes: DIC, haemolytic uraemic syndrome (HUS), TTP, disseminated carcinomatosis, malignant or pregnancy-induced hypertension (eclampsia)
Spherocytes	Small, densely packed RBC with loss of central pallor	Hereditary spherocytosis, autoimmune haemolytic anaemia, postsplenectomy
Sickle cell	Sickle shaped	Sickle-cell anaemia
Blister cells		Glucose-6-phosphate dehydrogenase deficiency
Nucleated RBC	Normoblasts	Bone marrow infiltration, severe haemolysis, myelofibrosis, acute haemorrhage
Polychromatia	Young red cells, reticulocytes (bluish tinge)	Haemolysis, acute haemorrhage, increased red-cell turnover

Q: What is **sideroblastic anaemia**?

A: Sideroblastic anaemias are inherited or acquired disorders characterized by refractory anaemia, a variable number of hypochromic cells in the peripheral blood, and excess iron and ring sideroblasts. Blood film usually shows microcytic anaemia; it may be dimorphic.

Classification:

1. **Hereditary:**
 a. X-linked disease, transmitted by female.
2. **Acquired:**
 a. Primary (one of the myelodysplastic syndromes).
 b. Secondary:
 - Inflammatory: Rheumatoid arthritis.
 - Neoplastic: Lymphoma, leukaemia, carcinoma, myeloproliferative disorders, multiple myeloma, carcinoma.
 - Drugs: Isoniazid (INH), pyrazinamide, ciclosporine.
 - Alcohol abuse.
 - Lead poisoning.
 - Other disorders, e.g. megaloblastic and haemolytic anaemias, malabsorption, severe malnutrition, erythroleukaemia.

Treatment:

- Treatment of the primary cause, if present, e.g. withdrawal of drug, stop alcohol intake, etc.
- Some cases may respond to pyridoxine, folic acid.
- Correction of anaemia by blood transfusion.

Q: What is **ring sideroblast**?

A: It is characterized by accumulation of iron in mitochondria of erythroblast around the nucleus, giving a ring-shaped appearance in the bone marrow.

CHAPTER 6

ENDOCRINOLOGY

"You see, but you do not observe"

– Sir Arthur Conan Doyle

Introduction

It is quite common that one may get a case related to endocrine disorders, more frequently than thyroid disorders; although other diseases are also not rare.

Remember, the diagnosis of endocrine disease may be obvious at your first observation of the patient. Hence, take a few seconds to have a quick look at the patient from head to foot carefully. Diagnosis of thyroid disorders (Graves disease and hypothyroidism) lies on the face of the patient. Also, Cushing syndrome and acromegaly are easily diagnosed by looking at the patient. Many a times, it is frequently asked, 'Look at the face. What is your diagnosis? What else do you want to examine?'

Underlying diagnoses by looking at the face may be:

- Graves disease (hyperthyroid, euthyroid or hypothyroid).
- Hypothyroidism (myxoedema).
- Cushing syndrome.
- Acromegaly.

Subsequent physical examination depends on your diagnosis. For example:

- If your diagnosis is thyroid disease, further clinical examination will be related to thyroid problems, e.g. signs of thyrotoxicosis, signs of hypothyroidism, examination of the eye, thyroid gland, etc.
- If your diagnosis is Cushing syndrome, examine other findings in relation to this (central obesity, striae, proximal myopathy and blood pressure).
- If acromegaly is suspected, then examine the face, hand, visual field, voice.

After an obvious diagnosis, the examiner may ask, 'What is the likely diagnosis? Ask some questions to the patient'.

In such a case, you must have a few **readymade questions** to be asked. For example:

- If Cushing syndrome is suspected, ask whether the patient is taking any steroid or experiencing weight gain, backache and difficulty in standing up after sitting.
- If hypothyroidism is suspected, ask whether the patient prefers warmth and has weight gain, increased sleep, constipation and so on.
- If hyperthyroidism is suspected, ask whether the patient has preference for cold and has excessive sweating, increased appetite but weight loss, irritability and so on.

Examination of Thyroid Gland

The usual instructions are:

- Examine the thyroid gland or the neck.
- Examine the thyroid status of the patient (you must see **signs of thyrotoxicosis** and also **signs of hypothyroidism)**.
- Look at the face (hypothyroid and exophthalmos). What else do you want to examine?

Proceed as follows:

1. Introduce yourself. While handshaking, check whether the hand is warm and sweaty.

2. Look at the patient's face:
 - Anxious, restless, fidgety and frightened face with staring looks (thyrotoxicosis).
 - Puffy face with periorbital swelling with baggy eyelids, loss of outer one-third of eyebrows and apathetic look (hypothyroidism).
 - Exophthalmos (bilateral or unilateral: Graves disease).
3. Then look (inspection), palpate and auscultate (thyroid).
 a. Inspection: Examine the neck both in front, left and right sides.
 - Obvious swelling (goitre): Ask the patient for deglutition (ideally patient should drink a glass of water). If any goitre, check whether it is diffuse, single or multinodular; and then check if one side is larger than the other.
 - Skin colour (redness indicates suppurative thyroiditis) and any scar of surgery.
 - Other obvious swelling (lymphadenopathy).
 b. Palpation (from back): Ask the patient to sit, ensure the neck is slightly flexed, palpate the gland with both hands and ask the patient to swallow again.

 If goitre is present, see whether it is unilateral or bilateral and diffuse or nodular (multinodular or single); then check the following points:
 - Size (which one is large, right or left).
 - Shape (diffuse or irregular).
 - Surface (smooth or irregular).
 - Consistency (soft or firm or hard).
 - Tenderness (if present, indicates subacute thyroiditis and suppurative thyroiditis).
 - Mobility.
 - Overlying skin condition.
 - Lower margin (to see retrosternal extension).
 c. Examine for retrosternal extension (prominent veins in neck and upper chest; feel the lower limit, tracheal deviation and percuss the upper part of chest for dullness. For Pemberton sign, see below).
4. Palpate the cervical lymph nodes (if palpable, suggest metastasis).
5. Feel for carotid pulse (absence of pulsation indicates malignant infiltration).
6. Finally, ask the patient to hold breath and auscultate for thyroid bruit (also carotid bruit and venous hum, which can be obliterated by gentle pressure at the root of neck). If thyroid bruit is present, check whether it is actually a murmur of aortic stenosis [ejection systolic murmur (ESM)] radiating from chest.

Finally, ask the examiner, 'I want to examine the thyroid status, eyes, pretibial myxoedema and heart'.

For **thyroid status**, see the **signs of thyrotoxicosis** and **signs of hypothyroidism**.

1. **Signs of thyrotoxicosis:**
 - Observe tremor of outstretched hands with fingers spread out. If no tremor is noted, put a paper over the fingers and note the tremor.
 - Palm: Warm and sweaty (in anxiety—palm is cold and sweaty).
 - Pulse: Tachycardia (better to record sleeping pulse).
 - Others: Generalized wasting, proximal myopathy and jerks exaggerated.

 N.B. There may be atrial fibrillation (AF), ectopics and high-volume pulse in thyrotoxicosis.

2. **Signs of hypothyroid2ism:**
 - Puffy face with periorbital swelling with baggy eyelids, loss of outer one-third of eyebrows and apathetic look.
 - Nonpitting oedema.
 - Pulse: Bradycardia.
 - Speech: Hoarse, croaky or husky voice.
 - Dry and thick skin.
 - Slow relaxation of ankle jerk.

Q: What are the **findings** in the eyes? What are the other **physical findings** to be seen?

A: Exophthalmos, lid lag, lid retraction and eye movement (see exophthalmos on page 455).

Other physical findings:
- Legs: Pretibial myxoedema (present only in Graves disease), reflex (may be exaggerated in thyrotoxicosis and slow relaxation of ankle jerk in hypothyroidism).
- Proximal myopathy (both upper and lower limbs) found in thyrotoxicosis (may be found in hypothyroidism also).
- Nails: Onycholysis in Graves disease.

Q: What is **Pemberton sign?**

A: It is a sign to see retrosternal extension of thyroid gland (also positive with any retrosternal mass). On raising both the arms above the head, the patient with retrosternal extension may develop the following signs of compression:

- Face: Suffusion or congestion and cyanosis.
- Respiratory distress (stridor).
- Neck veins are engorged.
- The patient may complain of dizziness and may be syncope. (This sign is rare, not specific for retrosternal goitre.)



Lid lag



Lid retraction



Pretibial myxoedema



Onycholysis in Graves disease

N.B. Remember the following points:

- Eye signs (exophthalmos, periorbital oedema, chemosis and diplopia), pretibial myxoedema and thyroid acropachy are present only in Graves disease. However, lid lag and lid retraction occurs in thyrotoxicosis due to sympathetic overactivity, which supplies levator palpebrae muscle.
- Thyroid bruit present in Graves disease.
- Other findings in hands in thyrotoxicosis include palmar erythema, onycholysis (separation of nails from bed called Plummer sign is present only in Graves disease) and clubbing (in case of thyroid acropachy—only in Graves).
- Exophthalmos and pretibial myxoedema do not correlate with toxicosis. It may be present both in hyper- or hypo- or euthyroid state associated with Graves disease.

Face in Thyroid Disease (by Looking at the Face)

The usual instructions are:

- Look at the face. What is your diagnosis? What else do you want to see? (Examine the face and also neck to see any goitre—whether diffuse or nodular. Examine from head to foot and observe generalized swelling of the body and nonpitting oedema.)

Presentation of a Case (Exophthalmos): Case No. 1

There is bilateral or unilateral exophthalmos.

- The patient looks anxious, restless and fidgety.
- Thyroid gland is diffusely enlarged.

Diagnosis is **Graves disease** with thyrotoxicosis.



Case no. 1: Graves disease

Q: What **else** do you like to see?

A: I want to see the signs of thyrotoxicosis. I want to examine the thyroid gland, eyes and legs (page 455).

Presentation of a Case (Myxoedema): Case No. 2 (a)

- The face is puffy with periorbital swelling and baggy eyelids, and appears apathetic.
- Outer one-third of the eyebrow is absent or reduced

My diagnosis is **myxoedema.**



Case no. 2 (a): Myxoedema (nongoitrous)

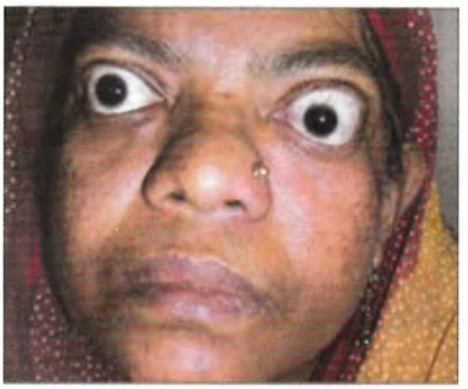
Q: What **else** do you like to see?

A: I want to see the signs of hypothyroidism. Also, I want to examine the thyroid gland, eyes, legs, skin, ankle jerk and nonpitting oedema. I want to talk to the patient.

Presentation of a Case (Myxoedema): Case No. 2 (b)

- As in Case no. 2 (a) **plus** there is bilateral exophthalmos.

My diagnosis is **hypothyroid Graves disease.**



Case no. 2 (b): Graves disease (hypothyroid)

Presentation of a Case (Myxoedema): Case No. 3

- As in Case no. 2, **plus** thyroid gland is diffusely enlarged, firm or rubbery, nontender, no bruit and no exophthalmos.

Diagnosis is **myxoedema** due to Hashimoto thyroiditis.



Case no. 3: Myxoedema (goitrous, Hashimoto thyroiditis)

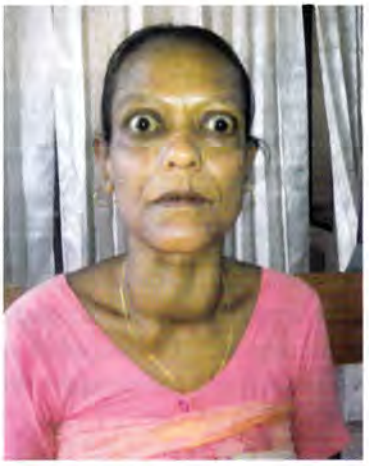
Thyrotoxicosis

Instruction by the examiner:

- Look at the patient. What else do you want to see?
- Examine the thyroid gland and relevants.

Presentation of a Case (Features of Thyrotoxicosis)

- The patient has tremor of outstretched hands.
- Palms of the hands are warm and sweaty.
- Pulse: 120/min (tachycardia). Pulse may be normal, if the patient is on β-blocker.



My diagnosis is **thyrotoxicosis.**

Q: What **else** do you want to examine?

A: I want to examine the thyroid gland, eye, cardiovascular system and jerks.

Q: What do you think the **cause** of thyrotoxicosis in this case?

A: As follows (mention the causes of that case by looking at face and neck):

- In young patient with diffuse goitre and exophthalmos, the likely cause is Graves disease (even if no exophthalmos, still it can be Graves disease).
- In the middle-aged with nodular goitre (single or multiple), the likely cause is toxic nodular or toxic multinodular goitre.

Causes of thyrotoxicosis

1. Graves disease: The commonest cause (76%).
2. Toxic multinodular goitre (14%).
3. Toxic nodular goitre (5%, toxic adenoma or hot nodule called Plummer disease).
4. Thyroiditis (subacute thyroiditis; also called De Quervain thyroiditis, and postpartum thyroiditis. All are transient).
5. Hashimoto thyroiditis (ultimately hypothyroidism develops).
6. Factitious thyrotoxicosis (self-intake of thyroxine).
7. Iodine induced (*Jod–Basedow phenomenon*) and drug (amiodarone).
8. Others (rare):
 - Carcinoma of thyroid (follicular).
 - Struma ovarii (secretes thyroid hormone).
 - Hydatidiform mole and choriocarcinoma [both secrete thyroid-stimulating hormone (TSH)].

Q: Ask a few **questions**. Or what **history** do you like to take in thyrotoxicosis?

A: Ask the patient:

- Do you prefer hot or cold? (Heat intolerance)
- Are you losing weight? (Weight loss common)
- How is your appetite? (Increased appetite)
- How is your bowel habit? (Diarrhoea may occur)
- In females, ask about menstruation (Usually amenorrhoea in thyrotoxicosis)

Others: Excess sweating, palpitation, tremor, irritability, insomnia and anxiousness or nervousness.

N.B. If any patient complains of loss of weight despite good appetite, the likely diagnosis is thyrotoxicosis. (Other cause may be diabetes mellitus (DM). However, loss of appetite in thyrotoxicosis may occur in the elderly.)

Q: What is **factitious thyrotoxicosis?**

A: Deliberate intake of T_4 to reduce weight, usually in emotionally disturbed person. Clues for diagnosis are high thyroid hormones and low radioiodine uptake. Thyroglobulin level is zero or low, high ratio of T_4:T_3 = 70:1 (in conventional thyrotoxicosis, the ratio is 30:1). Combination of negligible radioiodine uptake, high T_4:T_3 ratio and low thyroglobulin is diagnostic.

N.B. Remember the following points:

- The elderly may not have obvious features of thyrotoxicosis. The patient may present only with atrial fibrillation, tachycardia or heart failure, which masks thyrotoxicosis.
- Children may present with excess growth, behaviour problem like hyperreactivity, and increase in weight rather than loss.
- Apathetic thyrotoxicosis may be present in elderly patients with thyrotoxicosis, with features such as hypothyroidism. High degree of suspicion is essential.

Q: What **investigations** do you suggest in thyrotoxicosis?

A: As follows:

1. **To confirm thyrotoxicosis:**
 - FT_3, FT_4 and TSH (low TSH, high T_3 and T_4. But in T_3 toxicosis, TSH is low, T_4 is normal and T_3 is high).
 - Radioiodine uptake test (RAIU) and thyroid scanning (technetium scintigraphy is better than RAIU test because it is quicker to perform

and requires lower dose of radioactivity). RAIU shows rapid uptake and rapid turnover. There is high uptake in 2 or 4 and 24 h and rapid fall after 48 h.

2. **To find out causes:**
 - Ultrasonography of the neck (to see single, multinodular and diffuse goitre).
 - Thyroid autoantibody: For Graves disease TSH receptor stimulating antibody. Also, antiperoxidase and antithyroglobulin antibody (very high in Hashimoto thyroiditis, but slight-to-moderate high in Graves disease).
3. **Other tests:**
 - ECG.
 - Chest X-ray (retrosternal extension of goitre and cardiomegaly).
 - Blood sugar (secondary DM).
 - Serum cholesterol (low in thyrotoxicosis).
 - Fine-needle aspiration cytology (FNAC) (if goitre is present).
 - For ophthalmopathy (in Graves disease, see page 455).

Causes of thyrotoxicosis with low radioiodine uptake:

- Subacute thyroiditis (De Quervain thyroiditis).
- Postpartum thyroiditis.
- Factitious thyrotoxicosis.
- Iodine induced (patient on iodine or amiodarone, which contains iodine).
- Ectopic thyroid tissue producing thyrotoxicosis (struma ovarii, choriocarcinoma and hydatidiform mole).

Q: How to treat thyrotoxicosis?

A: Three modes of treatment: Drugs (carbimazole and propylthiouracil), radioiodine therapy and surgery.

Drug therapy:

1. Carbimazole or propylthiouracil: These drugs reduce the synthesis of thyroid hormones by inhibiting the iodination of tyrosine.
 - Carbimazole 45–60 mg daily. When the patient is euthyroid, reduce the dose; then 5–20 mg daily for 18–24 months. Periodic complete blood count (CBC) is necessary, as there may be agranulocytosis. Also, FT_4 and TSH should be measured.
 - Propylthiouracil 400–600 mg daily. Dose is reduced when the patient becomes euthyroid.
2. β-Blocker: Propranolol (up to 160 mg/day). It reduces sympathetic symptoms (such as tremor, tachycardia and sweating).

Indications of drug:

- Usually given in first episode in patient <40 years of age.
- Small goitre.
- Mild features of thyrotoxicosis.

Disadvantages of drugs:

- Relapse in 50% of the cases within 2 years of stopping the drug (surgery or radioiodine or long-term drug therapy may be needed in such case).
- Complication such as hypersensitive skin rash and agranulocytosis.
- Compliance may be poor.
- Costly.

N.B. Advise the patient with carbimazole therapy: If sore throat or fever develops, which may be due to agranulocytosis, stop the drug and inform the doctor.

Radioiodine therapy:

It acts by destroying the functioning thyroid cells and inhibiting their ability to replicate. Depending on the size of goitre, 5 to 10 mCi is given orally. It is effective in 75% cases in 4–12 weeks. In this period, propranolol is given. In severe cases, carbimazole may be given, which should be started 48 h after radioiodine therapy. If the drug is started before 48 h, it reduces the efficacy of radioiodine.

Indications of radioiodine therapy:

- Usually, above 40 years of age (however, some advocate to use in young).
- Recurrence after surgery or drugs, irrespective of age.
- Toxic multinodular goitre or toxic adenoma or hot nodule.
- In early age, with major serious other illness.
- Some cases of carcinoma thyroid (follicular, papillary after surgery).
- Ablative therapy with severe atrial fibrillation; also in heart failure.
- Psychosis.
- Poor drug compliance.
- Hypersensitivity to the drug.

Contraindications of radioiodine therapy:

- Pregnancy or planned pregnancy within 6 months of treatment.
- During lactation.
- Active or malignant Graves ophthalmopathy.

Disadvantages of radioiodine therapy:

- Hypothyroidism: It occurs in 40% in first year and 80% in 15 years.
- Early discomfort and exaggeration of hyperthyroidism may occur (due to radiation thyroiditis). Hence, the patient should be rendered euthyroid using drug, which should be stopped 2–5 days before radioiodine therapy.
- Exacerbation of ophthalmopathy.

N.B. In severe thyrotoxicosis, initially carbimazole is given for 4–8 weeks. Then radioiodine therapy is given. Carbimazole is stopped 48 h before radioiodine therapy. If no response after 12–24 weeks, a second dose of radioiodine is given.

Surgery (subtotal thyroidectomy):

The patient should be made euthyroid by antithyroid drug before operation. Potassium iodide should be added 60 mg 8 hourly, 2 weeks before operation. It inhibits thyroid hormone release, reduces the size and vascularity of gland, making surgery technically easier.

Indications of surgery:

- Large goitre or multinodular goitre.
- Relapse or no response to drug.
- Drug hypersensitivity.
- Noncompliance with drug.
- Suspicion of malignancy.
- Pressure effect.
- Cosmetic purpose.

Complications of surgery:

- Hypothyroidism in 25%.
- Transient hypocalcaemia (10%).
- Permanent hypoparathyroidism (1%).
- Recurrent laryngeal nerve palsy causing hoarseness of voice due to vocal cord palsy (1%).

N.B. In toxic nodular or multinodular goitre, treatment of choice is radioiodine therapy or surgery. Drug treatment is not helpful.

Q: What is thyrotoxic periodic paralysis (TPP)?

A: If a thyrotoxic patient develops sudden or periodic weakness, it is called TPP. It is due to hypokalaemia (caused by entry of potassium into the cell), common in Asians. It may occur following excess of carbohydrate or glucose or heavy exercise, and persists up to 7–72 h. Treatment of thyrotoxicosis improves the condition.

Q: How to treat thyrotoxicosis with atrial fibrillation?

A: AF occurs in 10% cases, common in the elderly of >60 years, more in toxic multinodular goitre, and may occur in subclinical hyperthyroidism. It is treated in the following ways:

- β-Blocker: Propranolol (digoxin has little role). Verapamil and amiodarone may be used, if β-blocker is contraindicated.
- Antithyroid drug, followed by radioiodine therapy.
- Anticoagulant: Aspirin in the elderly and warfarin in younger.
- 50% AF reverts spontaneously to sinus rhythm. If persistent, AF cardioversion may be done, provided T_4 and TSH are normal.

Q: How to treat thyrotoxicosis in pregnancy?

A: Pregnancy is unusual in thyrotoxicosis, as anovulatory cycles are common. Autoimmune thyroid disease is also less common, as maternal immune response is suppressed in pregnancy. Because of high thyroxine-binding globulin (TBG), total T_4 and T_3 are high, and TSH is low. Hence, high FT_4 and FT_3, and low TSH level suggest thyrotoxicosis. It is usually due to Graves disease. TSH receptor antibodies (TRAb) can cross placenta and develop thyrotoxicosis in foetus.

- Propylthiouracil is preferred (carbimazole can cross placenta causing foetal goitre and scalp skin defect in child called aplasia cutis). Propylthiouracil is given in lowest dose; less than 150 mg daily to prevent foetal hypothyroidism and goitre. TRAb is measured in last trimester; if not high, the drug can be stopped 4 weeks before delivery (to prevent neonatal hypothyroidism).
- If needed, propylthiouracil can be given after delivery and breastfeeding should be continued, as little is excreted in breast milk.
- If surgery is necessary, it should be done in middle trimester.

N.B. Radioiodine therapy is absolutely contraindicated in pregnancy.

Q: What is thyrotoxic crisis? How to treat?

A: Thyrotoxic crisis is characterized by life-threatening increase of signs and symptoms of thyrotoxicosis (also called thyroid storm).

Features of thyrotoxic crisis are:

- High fever.
- Restlessness, agitation and irritability.
- Nausea, vomiting, diarrhoea and abdominal pain.
- Tachycardia, AF and cardiac failure in elderly.
- Confusion, delirium and coma.

Precipitating factors for thyroid crisis:

- Infection.
- Stress.
- Surgery in unprepared patient.
- Following radioiodine therapy (due to radiation thyroiditis).

Diagnosis:

Mostly clinical and high degree of suspicion is vital. FT_3, FT_4 and TSH should be done immediately.

Treatment (blood sample taken for T_3, T_4 and TSH):

- The patient should be treated in intensive care unit (ICU).
- Propranolol 80 mg 6 hourly (or 1–5 mg IV 6 hourly).
- Intravenous (IV) fluid (normal saline and glucose).
- Carbimazole 40–60 mg daily. Or propylthiouracil 150 mg 6 hourly (if needed, through Ryle tube). Carbimazole can be given per rectally also.
- Other therapy: Sodium ipodate—a radiographical contrast media—500 mg daily is rapidly effective. Or potassium iodide or Lugol iodine may be given. Dexamethasone 2 mg 6 hourly and amiodarone are also effective.
- Broad-spectrum antibiotic.
- General measures: Control of temperature and O_2 therapy.
- After 10–14 days, the patient can usually be maintained on carbimazole alone.

Mortality rate in thyrotoxic crisis is 10%.

Graves Disease

Usual instructions are:

- Look at the patient. What are your findings? What else do you want to examine?
- Examine the thyroid gland.

(Remember, **Graves disease may be hyperthyroid, euthyroid and hypothyroid.**)

Presentation of a Case (Exophthalmos): Case No. 1

(See also page 455)

- There is unilateral or bilateral exophthalmos, periorbital oedema, chemosis, redness of eye, corneal ulceration, lid lag, lid retraction, ophthalmoplegia, and diplopia (mention if present).
- The face appears anxious, fidgety along with staring looks.
- Thyroid gland is diffusely enlarged, firm in consistency, nontender and mobile.
- There is bruit (mention the site).
- Signs of thyrotoxicosis are present (tachycardia, tremor, warm and sweaty palm).

Diagnosis is **thyrotoxicosis due to Graves disease**.

Q: Why it is Graves disease?
A: As there is exophthalmos and diffuse goitre.

Q: What else do you want to examine?
A: Dermopathy (pretibial myxoedema).

Q: What is the natural history of Graves disease?
A: It may be hyperthyroid and euthyroid, followed by hypothyroidism.

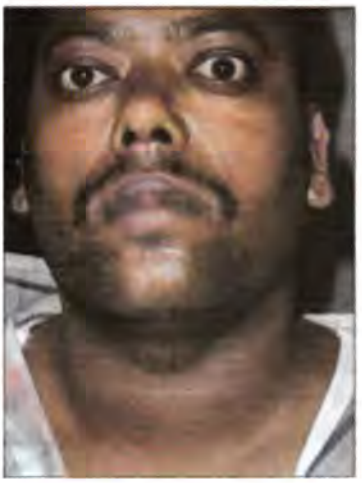
Presentation of a Case (Exophthalmos): Case No. 2

- There is unilateral or bilateral exophthalmos with no signs of thyrotoxicosis.

Diagnosis is **euthyroid Graves disease.**



Graves disease (thyrotoxicosis)



Graves disease (euthyroid)

Presentation of a Case (Exophthalmos): Case No. 3

- There is unilateral or bilateral exophthalmos.
- Coarse, puffy facies, periorbital puffiness and baggy eyelids. Patient looks immobile and uninterested.
- Skin is dry, cold and scaly.
- Nonpitting oedema and slow relaxation of ankle jerk.
- Voice: Coarse and croaky.

Diagnosis is **hypothyroid Graves disease.**

Q: What is Graves disease?

A: It is an autoimmune thyroid disease due to stimulating antibody to TSH receptors characterized by **triad** of:

- Exophthalmos.
- Diffuse goitre.
- Dermopathy (pretibial myxoedema).

Q: What is the cause of Graves disease?

A: Autoimmune disease due to IgG antibody against TSH receptor, producing excess thyroid hormones. TRAb acts similar to TSH. Common in female, M:F = 1:5. TRAb is of two types: (1) TSI, with 80–95% causing thyrotoxicosis and (2) TSH receptor-blocking antibody causing hypothyroidism.

Q: What is the **significance** of thyroid bruit? What is the **cause** of bruit?

A: It is pathognomonic of Graves disease and rarely occurs in other thyroid diseases. It indicates increased vascularity, probably due to an autoimmune mechanism.

Q: What is **euthyroid** Graves disease?

A: The patient is clinically and biochemically euthyroid, but there is ophthalmopathy. [Thyroid releasing hormone (TRH) stimulation test shows flat response curve.]

N.B. Remember, ophthalmopathy in Graves disease:

- Eye problems occur in 5–10% of the cases.
- Ophthalmopathy occurs in 50% in the first presentation, may develop after treatment of hyperthyroidism and precedes many years before hyperthyroidism.
- Not related to toxicosis. It may be present in euthyroid or hypothyroid.
- If hypothyroidism develops, exophthalmos may be aggravated, especially if treated with radioiodine therapy.
- Lid retraction resolves when the patient is euthyroid, but exophthalmos resolves slowly and may take up to 2–3 years.

Q: What is the **mechanism** of thyroid ophthalmopathy? What are the **changes** and how to **treat?**

A: It is immunologically mediated. Within the orbit, there is cytokine-mediated proliferation of fibroblast, which secretes hydrophilic glycosaminoglycans.

The following changes occur in ophthalmopathy:

- Excessive interstitial fluid and infiltration of chronic inflammatory cells in the orbit (lymphocytes, plasma cells and mast cells).
- Swelling and oedema of extraocular muscles.
- Increased retrobulbar pressure and eyeball is pushed forward (proptosis). In severe cases, optic nerve compression may occur.

Clinical features: Increased lacrimation, gritty sensation in the eye, pain due to conjunctivitis or corneal ulcer, reduced visual acuity and diplopia. It increases with poor control of thyroid function and also following radioiodine therapy. Ophthalmopathy is common in cigarette-smoking population. However, cigarette smoking is weakly associated with Graves disease.

Treatment:

- Reassurance and general treatment of the eye. Methylcellulose eye drops (relieves grittiness). To prevent exposure keratitis, use tinted glass and lateral tarsorrhaphy (if corneal ulcer).

- If visual field defect, loss of visual acuity and papilloedema or progressive exophthalmos is present, steroid in high dose (prednisolone 60–120 mg/day) may be helpful.
- Pulse methylprednisolone and cytotoxic drug (cyclophosphamide) may be helpful.
- In severe cases, irradiation of the orbit.
- If no response in 7–10 days or loss of visual acuity, orbital decompression may be necessary.
- For diplopia: Correction of eye muscle by surgery (but should be delayed for 6 months, until degree of diplopia is stable).

Q: Is there any evidence of **cancer** in Graves disease?

A: Unusual, but highly suspicious if there is associated cold nodule.

Eponyms of eye signs in thyroid disease

- Lid lag: Von Graefe sign.
- Absence of wrinkling of forehead on upward gaze: Joffroy sign.
- Impaired convergence of eye: Möbius sign.
- Infrequent blinking: Stellwag sign.
- Paralysis of extraocular muscles: Jendrassik sign.
- Weakness of at least one extraocular muscle: Ballet sign.

Q: What are the **investigations** and **treatment** in Graves disease?

A: See section on 'Thyrotoxicosis'.



Malignant exophthalmos (with chemosis)



Exophthalmos (less severe)

Q: What is **malignant exophthalmos?**

A: It is the severe, progressive exophthalmos, which may lead to blindness due to optic nerve compression. Treated with high dose of prednisolone up to 120 mg/day; it may require decompression or orbital irradiation.

Q: What is **pretibial myxoedema** (dermopathy)?

A: In this condition, there is firm, nodular, thickened or plaque-like lesion of pink or brown colour giving a peau d'orange appearance. Usually, present in the shin of legs up to the dorsum of foot (but may occur in any part of the body, especially at pressure point). It may be pruritic and hyperpigmented. It is present only in Graves disease in 10%, almost always associated with ophthalmopathy and is not a manifestation of hypothyroidism (pretibial myxoedema is a misnomer). Occasionally, pretibial myxoedema develops after treatment of hyperthyroidism, especially with radioiodine therapy. It is due to the deposition of mucopolysaccharide in the dermis.



Pretibial myxoedema (in shin)



Pretibial myxoedema (in dorsum of foot and shin)

Treatment is rarely necessary. Local injection of triamcinolone or ointment betamethasone may be helpful.

Q: How to treat Graves disease?

A: Graves disease is an autoimmune disease, which may present with hyper-, hypo- or euthyroid state.

- If there is thyrotoxicosis, medical, surgical or radioiodine therapy (discussed in thyrotoxicosis).
- If hypothyroidism, treat accordingly with thyroxin.
- In euthyroid cases, treatment is only symptomatic and supportive.

Simple Multinodular Goitre

Instruction by the examiner:

- Examine the neck.
- Examine the thyroid gland and relevant.

Presentation of a Case

- There is multinodular goitre; left lobe is larger than the right; and nodules are of variable size and shape, nontender, firm in consistency and freely movable.
- There is no bruit, no retrosternal extension and no cervical lymphadenopathy.
- The patient is clinically euthyroid (pulse—normal, no tremor, and no warm and sweaty palm).

My diagnosis is **simple multinodular** goitre.

Q: Why this is simple?

A: Because there are no features of thyrotoxicosis such as no tachycardia, no tremor of outstretched hand, and no warm and sweaty palm.

Q: What are the causes of simple multinodular goitre?

A: As follows:

- Iodine deficiency (the commonest cause).
- Drugs: Lithium, amiodarone and para-aminosalicylate (PAS).
- Thiocyanate in diet.

Q: How to investigate a multinodular goitre?

A: As follows:

- RAIU test. In iodine deficiency, there is high uptake and slow turnover. Otherwise, RAIU is normal.
- Thyroid scan.
- Ultrasonography (USG) of thyroid gland.
- FT_3, FT_4 and TSH (all normal; TSH may be high, due to iodine deficiency).
- FNAC of thyroid nodule (if cold nodule).
- In iodine deficiency, measurement of urinary iodine (<10 mg/dL) may be done.



Multinodular goitre (small size)



Multinodular goitre (huge and massive)

Q: What are the complications of multinodular goitre?

A: As follows:

- May develop thyrotoxicosis (toxic multinodular goitre).
- Compression: Such as dysphagia, hoarseness (due to involvement of recurrent laryngeal nerve), stridor and superior vena cava (SVC) obstruction.
- Severe pain due to haemorrhage in nodule.

Q: How to treat?

A: As follows:

- If small: Reassurance. Follow-up annually.
- If large or mediastinal compression or cosmetic reason: Partial thyroidectomy.

N.B. Remember the following points in multinodular goitre:

- Role of thyroxine: Not much effective and may cause toxicosis. Chance of malignancy is rare; usually it is benign. Malignancy may occur, if cold nodule.
- Common in middle-aged and elderly individuals.

Toxic Nodular or Multinodular Goitre

Instruction by the examiner:

- Examine the neck.
- Examine the thyroid gland and relevant.

Presentation of Case No. 1

- There is a nodule in the right lobe of thyroid, which is 3 × 2 cm in size, firm in consistency, nontender, smooth surface, freely movable, no bruit and no palpable lymph node.
- Signs of toxicosis are present (tachycardia, tremor of outstretched hand, warm and sweaty palm).

My diagnosis is **toxic nodular goitre.**

Presentation of Case No. 2

- Present as before (multinodular goitre).
- Signs of toxicosis are present (tachycardia, tremor of the outstretched hand, warm and sweaty palm).

My diagnosis is **toxic multinodular goitre.**

Q: What is the **natural history** of toxic multinodular goitre?

A: It is permanent and there is no spontaneous remission.

Q: How to **investigate** such a case?

A: As follows:

- FT_3, FT_4 and TSH (high T_3 and T_4, low TSH).
- RAIU test and thyroid scan (which shows rapid uptake and rapid turnover. There is high uptake after 2 and 24 h, falls after 48 h).
- USG of thyroid gland.
- Other tests (as described in thyrotoxicosis, such as ECG, chest X-ray, antithyroid antibody and so on).

Q: Which **single test** do you want to perform?

A: Single test is FT_3, as there may be only T_3 toxicosis; in such case, FT_4 and TSH may be normal or near-normal.

Q: How to **treat** toxic nodular or multinodular goitre?

A: As follows:

- β-Blocker (to reduce heart rate).
- Radioiodine therapy is a treatment of choice (high dose: 15–30 mCi). If severe toxicosis, antithyroid drug is given, followed by radioiodine therapy.
- Occasionally, surgery may be necessary, if there is large goitre. However, before surgery, patient should be made euthyroid.

N.B. Antithyroid drugs are given for short time. Long-term treatment with antithyroid drug is not helpful, as many nodules are autonomous and relapse is invariable after withdrawal of the drug.



Toxic multinodular goiter

Q: What are the **difference** between Graves disease and toxic multinodular goitre?

A: As follows:

Differences between Graves disease and toxic multinodular goitre

Features	Graves disease	Toxic multinodular goitre
Age	20–40 years	Middle-aged or elderly
Past history	Not specific	Nodular goitre for long time
Thyroid gland	Diffusely enlarged	Multinodular goitre
Cause	Autoimmune disease	Usually iodine deficiency

Differences between Graves disease and toxic multinodular goitre		
Ophthalmopathy	Common	Rare
Dermopathy	Common	Absent
Heart complications	Less common	More common
Thyroid acropachy	May occur	Absent
Hypothyroidism	May occur	Absent

Simple Diffuse Goitre

Instruction by the examiner:

- Examine the neck.
- Examine the thyroid gland and relevant.

Presentation of a Case

- Thyroid gland is diffusely enlarged, 5 × 4 cm, nontender, firm in consistency, freely mobile, has no bruit, no retrosternal extension and no palpable lymph node.
- There are no signs of toxicosis.

My diagnosis is **simple diffuse goitre.**

Q: Why is it **simple?**
A: Because there is no sign of toxicosis.

Q: What do you think are the **causes** in this case?
A: As follows:

- Iodine deficiency.
- If the patient is young, it may be puberty goitre.
- Goitrogens.

Q: What are the **presentations** of simple diffuse goitre?
A: Simple diffuse goitre is common in the second and third decade, 15–25 years, more in females (F:M = 3:1). The patient presents with swelling in the neck. Or only goitre is found during routine examination.

Sometimes, goitre is evident in pregnancy.



Diffuse goitre (simple)



Puberty goitre (simple)

Q: What are the **causes** of diffuse goitre?
A: As follows:

- Physiological: Puberty and pregnancy.
- Iodine deficiency (endemic goitre).
- Autoimmune: Hashimoto thyroiditis, Graves disease and postpartum thyroiditis.
- Goitrogens: Drugs (amiodarone, lithium, para-aminosalicylate (PAS) and phenylbutazone). Thiocyanate in diet (cabbage, cauliflower, turnips, soya beans, brussels sprouts).
- Iodide in large doses.
- Subacute thyroiditis (de Quervain thyroiditis).
- Dyshormonogenesis.
- Riedel thyroiditis.
- Suppurative thyroiditis.
- Infiltrative disease: Amyloidosis and sarcoidosis.

Q: How to **treat** simple diffuse goitre?
A: As follows:

- Mild-to-moderate: No treatment. Reassurance and follow-up. T_4 is sometimes helpful to shrink goitre.
- Treatment of primary cause.
- If large goitre is associated with pressure effect or cosmetic reason, surgery (partial thyroidectomy) may be done.

N.B. Clue for the diagnosis of different types of goitre:

- Diffuse and soft goitre, with exophthalmos: Suggestive of Graves disease.
- Diffuse and firm or rubbery hard goitre, with no exophthalmos: Suggestive of Hashimoto thyroiditis.
- Diffuse and soft: Suggestive of simple diffuse goitre.
- Diffuse, soft and tender: Suggestive of subacute thyroiditis.

Solitary Nodule or Simple Nodular Goitre

Instruction by the examiner:

- Examine the neck.
- Examine the thyroid gland and relevant.

Presentation of a Case

- There is a solitary nodule in the right (or left lobe), 2 × 2 cm, firm in consistency, nontender, smooth surface, freely movable, no bruit and no palpable lymph node.
- No signs of toxicosis.

My diagnosis is **simple nodular goitre.**

Q: What are the **causes of solitary thyroid nodule?**
A: As follows:

- Simple nodular goitre.
- Palpable nodule on diffuse or multinodular goitre.
- Thyroid cyst.
- Thyroid adenoma or toxic adenoma.
- Malignancy (carcinoma and lymphoma).

Q: What is the **nature** of solitary nodule?
A: Majority benign (80–90%); and some cases may be malignant (5–10%).

Q: Mention **one investigation.**
A: USG of thyroid.

Q: What **investigations** do you suggest?
A: As follows:

- USG (to see whether cystic or solid).
- RAIU and thyroid scan.
- FT_3, FT_4 and TSH.
- FNAC and open biopsy (if suspected malignancy).

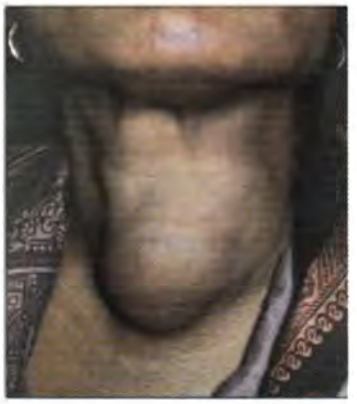
N.B. FNAC is the first investigation to be done in single thyroid nodule; accuracy is 70–97%.

Q: How to **treat** solitary thyroid nodule?
A: As follows:

1. 80% of the thyroid nodules are solid, cold, nontoxic and colloid. Treatment is:
 - Reassurance and follow-up.
 - Surgery for cosmetic purpose; or if suspicion of malignancy.
 - Thyroxin may be given in some cases.
2. 5–10% of the thyroid nodules are hot nodules. Treatment is:
 - Surgery or radioiodine therapy.
 - Ethanol injection into the nodule may be given.
3. Cystic nodule is usually benign. Aspiration is effective in 50% of the cases. Ethanol injection into the nodule is helpful. Thyroxin therapy is ineffective. Large cyst (>4cm) or cyst with bloody fluid usually recur and surgical excision should be considered.



Solitary nodule (right lobe)



Solitary nodule (isthmus)

Q: What are the **types** of benign adenoma?
A: They are of three types:

- Follicular (the commonest).
- Papillary.
- Hurthle cell type.

Q: How to **treat** benign adenoma?

A: As follows:

- If nonfunctioning: Reassurance and follow-up.
- Thyroxin may be given (if <4 cm, FNAC shows benign lesion and no risk factor for malignancy). Dose 2–3 mg/kg/day for 6 months. Re-evaluate. If no response, stop the therapy.
- Surgery: For cosmetic purpose or suspicion of malignancy.

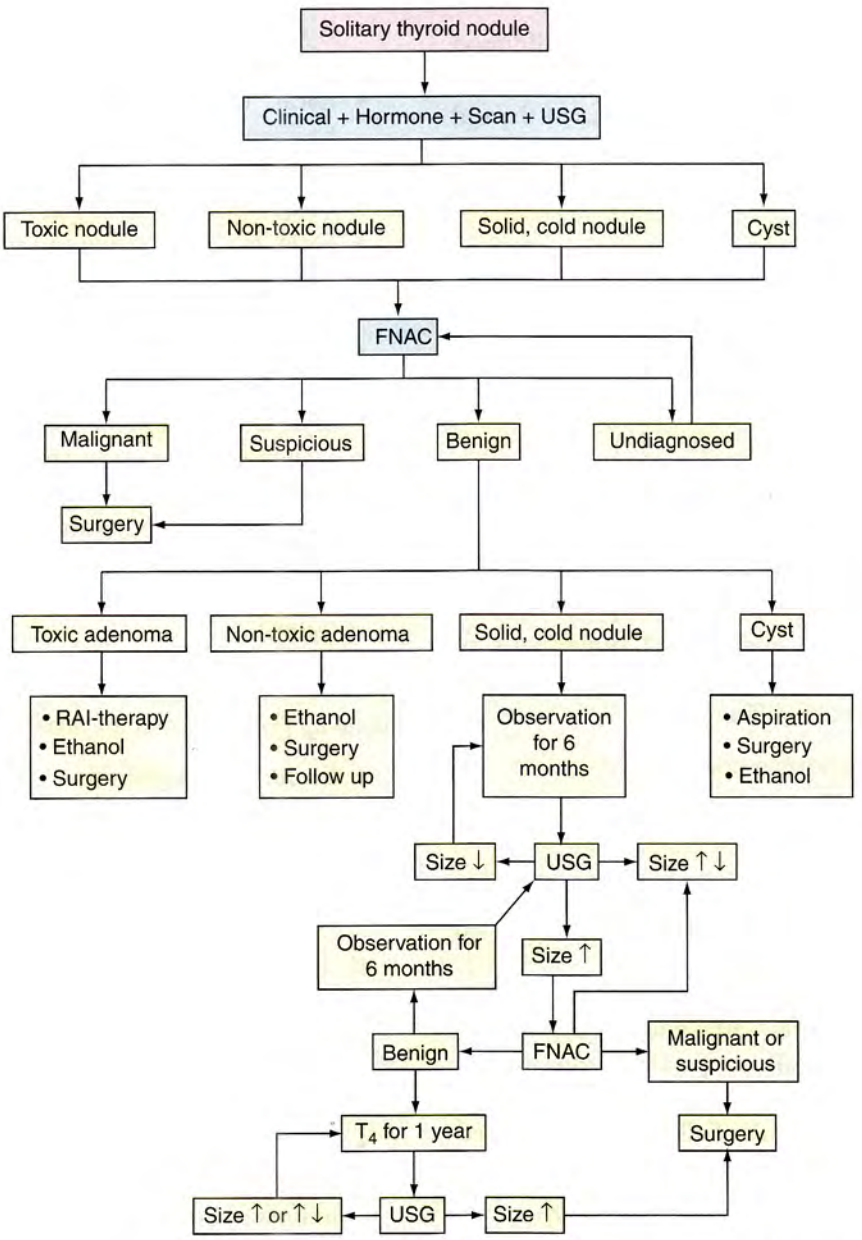
Q: What is **toxic** adenoma?

A: Thyrotoxicosis due to thyroid adenoma (usually follicular) called Plummer disease (no eye sign and no pretibial myxoedema). Thyroid scan shows hot nodule. It occurs in 5% of the cases of hyperthyroidism and is common in females of >40 years.

Treatment: Radioiodine therapy or surgery.

Q: How would you **investigate** a patient presenting with solitary thyroid nodule?

A: See the scheme below:



FNAC, fine-needle aspiration cytology; USG, ultrasonography cytology. *Courtesy*: Dr Md. Farid Uddin.

Q: What is the fate of untreated thyroid nodule?

A: As follows:

- May persist for long time.
- Spontaneous regression in 30%.
- Malignancy (5–10%).
- Cystic changes due to haemorrhage within the nodule.
- Secondary infection.

Q: How to suspect malignancy in a single thyroid nodule?

A: As follows:

- Age is elderly.
- History of recent and rapid growth.
- Hoarseness of voice.
- History of radiation therapy in childhood (in head and in neck).
- Family history [medullary carcinoma of thyroid (MCT)].
- Gland is solitary, hard, irregular and fixed to the underlying structures.
- Associated palpable lymph node.

Q: What are the types of nodules seen in thyroid scan?

A: They are of two types:

1. Nonfunctioning: Cold nodule.
2. Functioning:
 - Hot nodule: Only functioning nodule takes radioiodine; other parts of thyroid are suppressed.
 - Warm nodule: Functioning nodule and part of surrounding nodule show uptake.
 - Isofunctioning nodule and other parts of surrounding nodule show equal uptake; and both cannot be differentiated.

Q: How to treat functioning nodule?

A: As follows:

1. Hot nodule:
 - Radioiodine therapy: Better, especially after 40 years of age.
 - Surgery.
 - Local injection of alcohol: 1–2 mL weekly, 4–8 injections (80–90% effective).
2. Warm nodule: Follow-up. Local injection of alcohol may be considered.
3. Isofunctioning nodule: Follow-up. Local injection of alcohol may be considered.

Q: What are the types of thyroid malignancy?

A: Thyroid carcinoma is less common—1% of the malignancies. Usually, thyroid malignancy is associated with euthyroidism; occasionally hyperthyroidism.

All are common in females except MCT, which occurs equally in both sexes. The various types are:

- Papillary: 70–80% (the commonest).
- Follicular: 10%.
- Anaplastic or undifferentiated: 5%.
- MCT: 5–10%.
- Others: 5% (lymphoma and secondary deposit in thyroid).

Papillary carcinoma

- The commonest type; usually in young, 20–40 years. May be in later life (bimodal).
- It is slowly growing and multifocal, and makes up 90% of irradiation-induced thyroid cancer.
- Local lymph node metastasis is common; haematogenous spread is less common.
- Patient may present with cervical lymphadenopathy without thyroid enlargement.
- FNAC is very sensitive and specific test.

Treatment and prognosis:

- Total thyroidectomy followed by high-dose radioiodine therapy (to destroy remaining thyroid tissue and metastatic site).
- Lifelong T_4 (to suppress TSH, as it is TSH dependent).
- Prognosis is good; survival is almost the same as in normal person, if the lesion is localized; 20 years' survival in 95% (a potentially benign lesion).
- If distant metastasis, 40% survival up to 10 years.

***Follow-up** (following tests are done periodically):*

- Serum thyroglobulin. If raises, indicates recurrence or metastasis (normally, thyroglobulin is undetectable).
- Periodic whole-body scanning is done to check any metastasis.

If there is recurrence, high-dose radioablation should be done.

Follicular carcinoma

- Common in middle-aged, 40–60 years of age.
- Usually, a single encapsulated lesion.
- Blood-borne metastasis is common (to lung, brain and bone). Lymph node metastasis is rare.
- Diagnosis is done by open biopsy (FNAC is less specific).

- Treatment and follow-up: Exactly like papillary. Prognosis is good.
- Both follicular carcinoma and its secondary metastasis takes-up and responds to radioiodine therapy.

Anaplastic or undifferentiated carcinoma:

- Usually in the elderly, >60 years, more in women and highly malignant.
- Rapid thyroid enlargement of over 2–3 months. Goitre is hard.
- There may be hoarseness of voice due to recurrent laryngeal nerve palsy and stridor due to tracheal compression.
- If possible, perform surgery (total thyroidectomy and T_4 therapy).
- Resistance to almost any other treatment. Radiotherapy may be given.
- Survival is 6 months after diagnosis, if surgery is not possible.

Medullary carcinoma of thyroid (MCT):

- Arises from parafollicular C-cells, usually multifocal. May be inherited as autosomal dominant (AD) disease.
- Common in middle-aged and elderly, but may occur in young age when there is family history.
- Associated with multiple endocrine neoplasia (MEN) type-IIa (phaeochromocytoma and hyperparathyroidism) and -IIb (as in type-IIa plus multiple neuroma and Marfanoid body). May be sporadic too.
- Serum calcitonin is high (but no hypocalcaemia) and carcinoembryonic antigen (CEA) may be high.
- Also secretes histamine, serotonin, slow-reacting substance of anaphylaxis (SRS-A), prostaglandin and adrenocorticotropic hormone (ACTH).
- May cause carcinoid syndrome and Cushing syndrome.
- Lymph node metastasis is common and haematogenous spread is rare.
- Treatment: Total thyroidectomy with removal of affected lymph nodes and T_4 therapy. External radiotherapy may be given after surgery.
- Does not take radioiodine; chemotherapy is not effective.

Prognosis: Variable and relatively good. Some may survive up to 20 years, but some <1 year.

Lymphoma of thyroid:

- Rarely, may occur as primary or as a part of generalized lymphoma.
- Generally occurs in thyroid gland affected by Hashimoto thyroiditis. A rapidly enlarging mass in thyroid in patients with Hashimoto thyroiditis should arouse suspicion of lymphoma.

Treatment: External irradiation plus chemotherapy.

Hypothyroidism

Usual instructions are:

- Look at the face. What are your findings? What else do you want to examine?
- Examine the leg. What are your findings? What else do you want to examine?
- Examine the thyroid gland.

Proceed as follows:

- **Instruction 1:** Mention the findings of the face (see below). Then mention, 'I want to examine the legs (nonpitting oedema and slow relaxation of ankle jerk) and skin', talk with the patient (hoarse and croaky voice) and examine the thyroid gland.
- **Instruction 2:** Mention the findings in legs. Then mention, 'I want to examine the face, talk with the patient, and examine the skin and thyroid gland'.
- **Instruction 3:** Examine the thyroid gland systematically. Then mention, 'I want to examine the face, talk with the patient, and examine legs and skin'.



Myxoedema



Nonpitting oedema in myxoedema

Presentation of a Case (Only Myxoedema, No Goitre): Case No. 1

- The face is puffy with periorbital swelling, baggy eyelids and malar flush. There is also loss of outer one-third of eyebrows.
- Skin: Dry, rough, cold and thick (there may be yellow skin due to carotinaemia, vitiligo and erythema ab igne).
- Nonpitting oedema in leg and generalized swelling of whole body.
- Voice: Low pitched, slurred, hoarse and croaky (hypothyroidism is diagnosed by talking over telephone).
- Ankle jerk (slow relaxation).
- Pulse: 50/min (bradycardia).
- Thyroid gland (not enlarged).

My diagnosis is **myxoedema.**

Q: Ask some **questions** to the patient. Or, what **history** would you like to take?

A: When the patient answers, hear the voice and comment on it.

- Do you prefer hot or cold? (Cold intolerance)
- Are you gaining weight? (Increased weight gain)
- Tell me about your bowel habit (Usually constipation)
- In females: Ask about menstruation (Usually menorrhagia)

(Other history: Drug, thyroid surgery and radioiodine therapy to find out causes.)

Q: What do you think of the **cause** in this case (**nongoitrous** hypothyroidism)?

A: More likely **autoimmune** or **spontaneous atrophic.** Other possibilities are:

- Following radioiodine therapy.
- After surgery (check for any scar mark).
- Thyroid aplasia.
- TSH deficiency.

Presentation of a Case (Myxoedema with Goitre): Case No. 2 (a)

- Above findings in Case no. 1 **plus** there is a nodular goitre involving the isthmus of the thyroid gland, nontender, firm in consistency, freely movable and no bruit.

My diagnosis is **myxoedema, goitrous.**

Presentation of a Case (Myxoedema with Goitre): Case No. 2 (b)

- Above findings in Case no. 1 **plus** thyroid gland is diffusely enlarged, nontender, firm and rubbery, freely movable and has no bruit.

My diagnosis is **myxoedema.**

Q: What do you think of the **causes (goitrous hypothyroidism)**?

A: Hashimoto thyroiditis.

Q: What are the **other causes** of hypothyroidism in this case?

A: Other possibilities are:

- Drugs: Lithium, amiodarone and iodide.
- Endemic iodine deficiency (less common).
- Rarely, dyshormonogenesis and infiltrative disease (amyloidosis and sarcoidosis).



Case no. 1: Myxoedema (nongoitrous)



Case no. 2 (a): Myxoedema
(goitrous—nodular)



Case no. 2 (b): Myxoedema
(Hashimoto thyroiditis—diffuse goitre)



Case no. 3: Myxoedema
(Graves disease showing exophthalmos)

Presentation of a Case (Myxoedema with Graves Disease): Case No. 3

- Above findings in Case no. 2 **plus** there is bilateral exophthalmos and pretibial myxoedema.

My diagnosis is **Graves disease with hypothyroidism** (for details see Graves disease).

Q: Why **hypothyroidism** in Graves disease?

A: Natural history of Graves disease is hyperthyroidism, followed by euthyroidism and hypothyroidism. (This may occur following radioiodine therapy or after surgical treatment.)

Q: What are the **causes** of hypothyroidism?

A: As follows:

1. Autoimmune:
 - Hashimoto thyroiditis.
 - Spontaneous atrophic hypothyroidism.
 - Graves disease (associated with TSH receptor-blocking antibody).
2. Iatrogenic:
 - Radioiodine therapy for thyrotoxicosis.
 - After surgery (thyroidectomy).
 - Postradiotherapy in neck.
 - Drugs: Lithium, amiodarone and antithyroid drug therapy.
3. Others:
 - Endemic iodine deficiency.
 - Postpartum thyroiditis.
 - Rarely, dyshormonogenesis.
 - Secondary to hypopituitarism and hypothalamic disorders (rare).

Q: What are the causes of **goitrous** hypothyroidism?

A: As follows:

- Hashimoto thyroiditis.
- Graves disease (in such case, there is also exophthalmos and diffuse goitre with dermopathy).
- Endemic iodine deficiency (less common).
- Drugs: Lithium, amiodarone, iodide.
- Rarely, dyshormonogenesis.

Q: What are the causes of **nongoitrous** hypothyroidism?

A: As follows:

- Autoimmune or idiopathic (spontaneous atrophic)—commonest cause.
- Following radioiodine therapy for thyrotoxicosis.
- Postradiotherapy in the neck.
- After surgery (thyroidectomy).
- Secondary to hypopituitarism, hypothalamic disorders.



Juvenile hypothyroidism



Cretinism

Q: What is **cretinism?**

A: It is defined as hypothyroidism due to congenital deficiency of thyroid hormone, also called congenital myxoedema. Features are as follows:

1. Features in neonates:
 - Prolonged physiological jaundice.
 - Hoarse cry.
 - Lethargy.
 - Constipation.
 - Feeding problem.
 - Hypotonia.
2. Features in older babies are:
 - Characteristic facies: Dull and so-called idiotic look, large head, sparse hair, broad flat nose with big nostrils, widely set eyes (hypertelorism), thick everted lips with macroglossia.
 - Pot-belly with umbilical hernia.
 - Skin is dry, scaly, rough, cold and pale yellow (carotenaemia). Hair is sparse, coarse and rittle.
 - Delayed developmental milestones such as delayed dentition, delayed crawling, etc.
 - Hoarse voice.
 - Short stature.
 - Thick and short neck with presence of supraclavicular pad of fat.
 - Lethargy and hypotonia.
3. In older children, typical features of hypothyroidism are present.

In the early age, high degree of suspicion is essential for the diagnosis. Routine screening of neonates using a blood spot for TSH is done for diagnosis. T_4 should be started immediately. If treatment is delayed, permanent neurological and intellectual damage may occur.

Q: What **investigations** should be done to diagnose myxoedema?

A: As follows:

1. Serum FT_3, FT_4 and TSH (both T_3 and T_4 are low, TSH is high).
2. Autoantibody (for Hashimoto thyroiditis): Antiperoxidase and antithyroglobulin (both are very high).
3. Other tests (not for diagnosis, but to check other effects):
 - ECG (low-voltage tracing, sinus bradycardia and T-wave inversion).
 - Chest X-ray (cardiomegaly due to pericardial effusion and heart failure).
 - Serum cholesterol and triglyceride (high).
 - Creatinine phosphokinase (CPK), lactate dehydrogenase (LDH) and serum glutamic oxaloacetic transaminase (SGOT). (All may be high; these are not done routinely.)

Q: What **single investigation** should be done in myxoedema?

A: Single test is TSH and other one is T_4. But T_3 sometimes may be normal, as it is converted from T_4.

Q: What are the thyroid functions in **secondary** hypothyroidism?

A: Low FT_3, FT_4 and TSH (usually all thyroid hormones are low.)

Q: If a patient has **low** T_3, T_4 and TSH, what are the causes? How to investigate **in such case?**

A: Causes may be in the pituitary or hypothalamus. TRH stimulation test should be done.

- After giving TRH, if TSH is high, the cause is in the hypothalamus.

- If there is no or little rise of TSH, the cause is in the pituitary.

Q: What is the **treatment of hypothyroidism**?

A: Thyroxine: It should be started with low dose. The dose should be increased gradually after 3 weeks. Single dose is preferable and should be taken before breakfast. TSH should be repeated after 6–8 weeks. Once TSH is normal, maintenance dose should be continued as a single daily therapy. For follow-up, annual thyroid function test should be done.

N.B. If the patient has deficiency of cortisol (as in hypopituitarism or Addison disease), corticosteroid should be given first and then thyroxine. Otherwise, if thyroxine is given first without correcting cortisol deficiency, there will be severe Addisonian crisis.

Q: Why **thyroxine** should be started in low dose?

A: Because if high dose is given, it may precipitate anginal attack.

Q: **How long** will you continue the treatment?

A: Lifelong.

Q: If the patient has **ischaemic heart disease** with hypothyroidism, how to treat?

A: As follows:

- Thyroxine should be given in low dose (25 µgm). Dose should be increased slowly up to the optimum dose.
- β-Blocker (propranolol) should be added.
- Coronary dilator, calcium antagonist may be added.
- Coronary angiography followed by angioplasty or coronary artery bypass surgery may be needed.

Q: What are the causes of **transient** hypothyroidism? How to treat?

A: Causes are:

- Subacute thyroiditis.
- Postpartum thyroiditis.
- Drug induced.

Temporary T_4 therapy may be given. Follow-up with measurement of TSH should be done.

Q: How to investigate and treat **hypothyroidism in pregnancy**?

A: Hypothyroidism is difficult to diagnose in pregnancy, as normal pregnancy may be associated with many features of hypothyroidism such as cold skin, cold intolerance, weight gain, constipation. High degree of suspicion is essential.

- Most sensitive investigation is TSH, which is high. Also, FT_3 and FT_4 should be done (total T_3 and T_4 may be high in normal pregnancy due to increase TBG).
- Treatment: Thyroxine should be given (100–150 µgm once daily). Requirement of thyroxine is relatively high (40–50%) in pregnancy because of increased metabolism of thyroxine by the placenta and also increased serum TBG in pregnancy, which binds thyroxine, resulting in less FT_3 and FT_4.
- Dose of thyroxine should be adjusted to maintain normal TSH (serum TSH and FT_4 should be measured during each trimester).

Q: How to treat an **elderly** patient with hypothyroidism?

A: Treatment is the same. But one should take care whether the patient is suffering from any ischaemic heart disease. Following thyroxine, it may precipitate angina and myocardial infarction. Treatment is the same as above.

Read the Following Topics in Relation to Hypothyroidism

Q: What **bedside test** will you do in myxoedema?

A: Ankle jerk. There is slow relaxation called **hung-up reflex** (other jerks may show slow relaxation).

Q: How is slow relaxation **best elicited** in the ankle? **Why** slow relaxation?

A: Best elicited by kneel-down position on a chair or bedside. It is due to decreased muscle metabolism.

Q: Why **nonpitting** oedema?

A: Due to deposition of mucopolysaccharide substances, hyaluronic acid and chondroitin sulphate. These are also responsible for hoarse voice, carpal tunnel syndrome and body swelling.

Q: What is the **difference** between myxoedema and hypothyroidism?

A: Myxoedema is severe form of hypothyroidism due to deposition of mucopolysaccharide substances; but all hypothyroidism may not be myxoedematous.

Q: What are the **types** of anaemia in hypothyroidism?

A: Anaemia may be:

- Usually, normocytic normochromic.
- Iron deficiency, if menorrhagia (in female).
- May be macrocytic due to associated pernicious anaemia.

Q: What are the **causes** of anaemia in hypothyroidism?

A: Causes of anaemia:

- Anaemia of chronic disorder.
- Iron deficiency.
- Vitamin B_{12} deficiency.
- Folate deficiency.
- Other factors responsible: Menorrhagia in female, anorexia.

N.B. Macrocytosis in peripheral blood; but normoblastic bone marrow occurs in hypothyroidism.

Q: What is the **difference** between primary and secondary hypothyroidism?

A: As follows:

- Primary hypothyroidism involves thyroid gland associated with myxoedema.
- Secondary hypothyroidism is due to the involvement of pituitary or hypothalamus. In such cases, myxoedema is rare; there are other features of hypopituitarism.

Q: What is **subclinical hypothyroidism** (borderline hypothyroidism or compensated euthyroidism)?

A: In this condition, T_3 and T_4 are in the lower limit of normal and TSH is slightly high. The patient may be clinically euthyroid. This may persist for many years, though overt hypothyroidism may occur. Conversion to overt hypothyroidism is more common in men or when thyroid peroxidase (TPO) antibody is present or when TSH level is more than 10 mU/L.

Treatment: Thyroxine therapy may be given if TSH is persistently raised above 10 mU/L or when there are symptoms or high titre of thyroid antibodies or lipid abnormalities. If only TSH is marginally high with vague symptoms, thyroxine may be given sometimes. However, in female TSH should be normalized during pregnancy to avoid any adverse effect in foetus.

If TSH is marginally raised, the test should be repeated after 3–6 months.

Q: What are the **cardiovascular problems** in myxoedema?

A: As follows:

- Sinus bradycardia.
- Pericardial effusion.
- Congestive cardiac failure.
- Ischaemic heart disease.
- Hypertension
- Atherosclerosis (because of hypercholesterolaemia).

Q: What are the **neurological features** in hypothyroidism?

A: As follows:

1. Carpal tunnel syndrome (or tarsal tunnel syndrome).
2. Slow relaxation of ankle jerk.
3. Psychosis (myxoedema madness).
4. Myxoedema coma.
5. Cerebellar syndrome.
6. Deafness (Trotter syndrome).
7. Others:
 - Epileptic fit (due to SIADH).
 - Peripheral neuropathy.
 - Myotonia (Hoffman syndrome).
 - Proximal myopathy.
 - Pseudodementia.
 - Drop attack.

Q: What is **sick euthyroid syndrome?**

A: In any severe acute nonthyroidal illness or after surgery, there may be abnormal thyroid function test; although the patient is euthyroid—called sick euthyroid syndrome. It may occur after myocardial infarction, pneumonia, cerebrovascular disease (CVD) and drugs (dopamine and steroids). Usually, there is low TSH, high T_4, and normal or low T_3. Levels are usually mildly below normal and are thought to be mediated by interleukins (IL-1 and IL-6). Test should be repeated after recovery of systemic illness. Biochemical thyroid function should not be done in patients with acute nonthyroidal illness, unless there is good evidence of thyroid disease (such as goitre and exophthalmos).

Mechanisms of sick euthyroid syndrome:

- Reduced production or affinity of TBG to T_4 and T_3.
- Reduced peripheral conversion of T_4 to T_3; occasionally, more rT_3 (inactive reverse T_3).
- Reduced hypothalamic pituitary TSH production; hence low T_3 and T_4.

Q: What is **Hoffman syndrome?**

A: In myxoedema, there may be myotonia with pain and swelling in the muscles after exercise called Hoffman syndrome.

Q: What is **Pendred syndrome?**

A: It is an inherited disorder [autosomal recessive (AR)] associated with sensorineural deafness and goitre. It is due to the inborn error of thyroid hormone synthesis.

Q: What is **myxoedema coma?** What are the **mechanisms?** How to **treat?**

A: Myxoedema coma is characterized by depressed level of consciousness or even coma. Convulsion

may occur. It is rare; may occur in severe hypothyroidism, usually in elderly. Cerebrospinal fluid (CSF) studies show high pressure and high protein content. There is 50% mortality.

Causes of myxoedema coma:

- Syndrome of inappropriate ADH secretion (SIADH). Coma is due to hyponatraemia.
- Hypoxaemia.
- Hypercapnia.
- Hypothermia.
- Hypoglycaemia.
- Other factors: Cardiac failure, infection, use of sedative.

Treatment of myxoedema coma: It is better to be treated in ICU. Before starting treatment, blood is taken for FT_3, FT_4, TSH and cortisol.

1. T_3 (rapidly acting) 20 µgm, 8 hourly usually IV given (parenteral T_4 is not available; also slow-to-start action). If parenteral T_3 is not available, oral thyroxine through Ryle tube should be given.
2. IV hydrocortisone: 100 mg 8 hourly (especially if suspicion of hypopituitarism).
3. Other treatment:
 - Slow rewarming.
 - High-flow O_2 therapy.
 - IV fluid and glucose.
 - Antibiotic.
 - Assisted ventilation may be necessary (as in any unconscious patient).

Q: What is **myxoedema madness?**

A: It may occur in severe hypothyroidism in the elderly. There is dementia or psychosis, sometimes with delusion. Sometimes, these features may occur shortly after starting thyroxine replacement. Depression is common in hypothyroidism.

Q: What is **Hashimoto thyroiditis?**

A: It is an autoimmune thyroiditis characterized by destructive lymphoid infiltration of thyroid leading to atrophic change with regeneration and goitre formation. It is more common in middle-aged woman.

- The goitre is usually diffuse, moderately enlarged, and firm or rubbery. Sometimes, it may be soft-to-hard.
- Antithyroid antibody (very high, >1000 IU/L): Antimicrosomal (antiperoxidase) in 90% and antithyroglobulin antibodies (no rise of TSH-receptor antibody).
- About 25% patients are hypothyroid at presentation. In the remaining patients, serum T_4 is normal and TSH is normal or raised. There is a risk of developing overt hypothyroidism in future. Initially, the patient may present with features of toxicosis called Hashitoxicosis.
- In young patients (<20 years), ANF may be positive.
- Since this is an autoimmune disease, it may be associated with other autoimmune diseases like Addison disease, DM, premature ovarian failure, rheumatoid arthritis, Sjogren syndrome, ulcerative colitis, autoimmune haemolytic anaemia.
- Treatment: Thyroxine (it reduces the size of goitre also).

Q: What is the **radioiodine uptake** in Hashimoto thyroiditis?

A: It shows the following:

- Initially: Increased (toxic phase).
- After few days or weeks: Normal uptake.
- Later on: Less uptake (hypothyroid phase).

Q: What are the **histological** findings in Hashimoto thyroiditis?

A: As follows:

- Lymphocyte infiltration; also monocyte and plasma cell.
- Hyperplasia and fibrosis.
- Hurthle cell.

Q: What are the **autoimmune diseases** associated with thyroid disorder?

A: Thyroid disorders may be associated with autoimmune diseases like pernicious anaemia, Addison disease, Sjögren syndrome, DM, autoimmune haemolytic anaemia, systemic lupus erythematosus (SLE), autoimmune hepatitis, primary biliary cirrhosis (PBC) and premature ovarian failure.

Acromegaly

Usual instructions are:

- Look at the patient. What is the diagnosis? What else do you want to examine?
- Examine the hands of the patient. What is your diagnosis? Perform the general examination of the patient.

Presentation of a Case (by Looking at the Patient): Case No. 1

- Large coarse facies with prominent supraorbital ridge, more wrinkling of forehead and baggy eyelids.
- Large jaw, mainly lower; large lips, nose and ears.
- Teeth show malocclusion and are widely apart with prognathism (protrusion of lower jaw forward; hence the lower teeth overbites the upper teeth).
- Large tongue (macroglossia).
- Skull enlarged (look for any frontal craniotomy scar).



Acromegaly

My diagnosis is **acromegaly**.

Q: What else do you want to examine in this case?
A: As follows:

- Hands (shake hands): See below.
- Also examine the legs: Large feet.
- Eyes: Bitemporal hemianopia (see visual field).
- Skin: Thick, greasy and sweaty.
- Other parts of body: Enlarge as a whole.
- Talk with the patient: Husky and cavernous voice (due to the enlargement of larynx).
- Axilla: Acanthosis nigricans and skin tag (molluscum fibrosum).
- Others: Kyphosis, arthritis, gynaecomastia, coarse hair, cardiomegaly and thyromegaly.
- Check BP (high).
- Examine the urine for sugar (secondary DM may occur).



Large face and jaw

Presentation of a Case (by Examining the Hands): Case No. 2

- Both hands are large, warm and sweaty, doughy feeling, spade-like fingers.
- Carpal tunnel syndrome (if asked to examine the hands, always test for it).
- Clubbing present.



Spade-like hands

My diagnosis is **acromegaly**.



Large foot



Widely apart teeth with prognathism (front view)



Prognathism (side view)

Q: What are the changes in the eyes in acromegaly?

A: Bitemporal hemianopia (due to pressure on optic chiasma). Also, optic atrophy, papilloedema and angioid streaks in retina.

Q: What is acromegaly?

A: Acromegaly is characterized by generalized enlargement of the whole body. It is due to excess growth hormone secretion from pituitary macroadenoma (>10 mm) after union of epiphysis. If occurs before the union of epiphysis, it is called gigantism.

Q: Why it is called acromegaly?

A: Because of the enlargement of peripheral (acral) parts of body (*acro* means periphery or limbs and *megaly* means big).

Q: Can acromegaly and gigantism exist together?

A: Yes, if excess growth hormone starts in adolescence and persists in adult life, the two conditions may be present together.



Gigantism

Q: What is the cause of acromegaly?

A: Eosinophilic adenoma of pituitary (macroadenoma) causing excess growth hormone (GH) secretion after fusion of epiphysis. Rarely, ectopic production of growth hormone-releasing hormone (GHRH) may cause acromegaly (pancreatic islet cell tumour, oat cell carcinoma of bronchus and medullary carcinoma of thyroid).

Q: What are the causes of prominent supraorbital ridge?

A: As follows:

- Rickets.
- Paget disease.
- Achondroplasia.
- Hydrocephalus.
- Hereditary haemolytic anaemia.

Q: What are the **causes of macroglossia**?
A: As follows:

- Acromegaly.
- Hypothyroidism.
- Amyloidosis.
- Down syndrome.

Q: What are the **causes of baggy eyelids**?
A: As follows:

- Old age.
- Myxoedema.
- Acromegaly.
- Alcoholism.
- Nephrotic syndrome or acute glomerulonephritis.

Q: What are the **presentations** of acromegaly?
A: As follows:

- Progressive increase of the size of the body (there may be a history of change in size of rings, shoes, hats).
- Weight gain but weakness.
- Visual field defect (the patient gives history of collision with doors, persons because of the defective temporal field of vision).
- Headache (common).
- Excessive sweating.
- Features of hypertension, DM.
- Patient may give history of frequent visit to the dentist.
- Sleep apnoea syndrome.

Q: What are the signs of **active acromegaly**?
A: Signs of activity:

- Progressive increase in the size of the body.
- Excessive sweating.
- Increasing visual field defect.
- Large skin tags (Molluscum fibrosum).
- Presence of glycosuria (DM).
- Hypertension.
- Progressive headache.
- Enlarging thyroid.

N.B. Long-term **complications** of acromegaly:

- Increased incidence of large bowel carcinoma.
- Increased atherosclerosis.

Q: What are the **causes of death** in acromegaly?
A: As follows:

- Heart failure.
- Complications of hypertension.
- Degenerative vascular disease.
- Tumour expansion (mass effect).
- Pituitary apoplexy: Rapid expansion of pituitary tumour due to infarction or haemorrhage within the tumour. The patient complains of sudden severe headache and loss of consciousness (require immediate neurosurgical intervention).

Q: What are the **investigations** done in acromegaly?
A: As follows:

1. Radiology:
 - Skull X-ray: It shows enlarged sella turcica, erosion of clinoid process, enlarged skull, mandible and sinuses.
 - X-ray of the hands: There is large soft tissue, bones, widening of joint space and tufting of terminal phalanges.
 - X-ray of the foot: To see heel pad (normally, in male up to 21.5 mm and in female: 18 mm; if >25 mm, highly suggestive). Other changes like hand.
 - Other X-rays: Knee joint and chest X-ray.
2. GH assay (radioimmunoassay): Normally, <1 mU in adult (except in stress).
3. Glucose tolerance test (GTT) with simultaneous measurement of GH (more diagnostic): Normally during GTT, there is suppression of GH <2 mU. In acromegaly, there is failure of suppression of GH; occasionally there is paradoxical rise of GH.
4. Measurement of insulin-like growth factor-1 (IGF-1) (also called somatomedin-C) usually increases.
5. CT scan or MRI of the skull (MRI is more preferable).
6. Others:
 - Assessment of other anterior pituitary hormones.
 - Comparison with old photographs.
 - Perimetry (to see bitemporal hemianopia).
 - Blood sugar: DM in 10% cases; **IGT** in 25% cases.
 - ECG.
 - Serum calcium (increases in MEN).

Q: What is the **treatment** of acromegaly?
A: As follows:

1. Surgery:
 - Trans-sphenoidal removal of microadenoma is the treatment of choice (there is high success rate, rapid reduction of growth hormone and low incidence of hypopituitarism). Cure rate is 80% in microadenoma and 40% in macroadenoma.

- After 3 months postoperative, measure growth hormone and pituitary-function tests. If growth hormone remains high, adjuvant medical or radiotherapy may be needed.
- Occasionally, transfrontal surgery is done in large macroadenoma with suprasellar extension. Total removal of tumour may not be possible due to more complications. Postoperative radiotherapy should be given.

2. Radiotherapy:
 - It is used as a second-line therapy. External irradiation by linear accelerator is given in acromegaly, which persists after surgery to stop the tumour growth and to lower growth hormone levels. However, growth hormone level falls very slowly over many years. (Previously implantation of Yttrium was used.)
 - Radiotherapy can be used in combination with somatostatin analogue or dopamine agonist because of slow biochemical response to radiotherapy.
3. Drugs: Given if surgery is not possible or there is persistent acromegaly after surgery.
 - Somatostatin analogue (octreotide or lanreotide) may be used as a slow-release injection, every 2–4 weeks.
 - Bromocriptine: It is a dopamine agonist, given in high dose, which reduces GH level and the size of tumour. But it is less potent in lowering growth hormone and recurs after withdrawal of drug. Its main side effects are nausea, vomiting and postural hypotension. Alternatively, cabergoline 0.5 mg/day may be given or quinagolide may be used.
 - A peptide GH receptor antagonist (pegvisomant) may be used.
4. Other treatment:
 - Control of hypertension and DM (both improve with the treatment of acromegaly).
 - Cardiac problems: Whether it improves with the treatment of acromegaly is not clear.

N.B. Aim of treatment is to reduce the growth hormone level below 5 mU/L, which shows reduced mortality. A normal IGF-1 level is also a goal of therapy. So, the progress can be assessed by monitoring growth hormone and IGF-1 level.

Q: How to assess the **response of therapy** in acromegaly?

A: As follows:

- Clinical improvement (decreased facial puffiness, body size, less sweating, improvement of hypertension and DM).
- Progress can be assessed by GH and insulin-like growth factor (IGF-1) measurement.

Brief Discussion Regarding Hyperprolactinaemia

Q: What are the causes of **hyperprolactinaemia?**

A: As follows:

1. Physiological: Severe stress, pregnancy, lactation, exercise, coitus and sleep.
2. Drugs:
 - Dopamine antagonist group of drugs:
 - Antipsychotic (phenothiazine, butyrophenones).
 - Antiemetic (metoclopramide, domperidone).
 - Antidepressant.
 - Dopamine-depleting drugs (methyldopa).
 - Oestrogen therapy (e.g. oral contraceptive pill)
3. Pathological:
 - Prolactinoma (usually microadenoma <10 mm).
 - Pituitary macroadenoma.
 - Macroprolactinaemia (there is high prolactin without clinical features of hyperprolactinaemia).
 - Primary hypothyroidism.
 - Polycystic ovarian syndrome.
 - Rarely: Renal failure, liver failure, hypothalamic tumour, ectopic tumour, postictal state, chest wall injury or reflex (e.g. postherpes zoster).
 - Idiopathic.

Clinical features of hyperprolactinaemia:

- Galactorrhoea, hypogonadism (commonest symptoms).
- In male: Decreased libido, impotence, lethargy.
- In female: Amenorrhoea, oligomenorrhoea, menorrhagia, infertility.

Investigations:

- Serum prolactin (very high).
- CT or MRI of brain.
- Other investigations according to the suspicion of cause, e.g. thyroid function, renal function.

N.B. Remember the following points:

- If serum prolactin is high, repeat measurement is indicated to reconfirm.
- If serum prolactin is in the range of 500–1000 mU/L, it is more likely due to stress or drugs.
- If serum prolactin is in the range of 1000–5000 mU/L, it may be due to stress or drugs or microadenoma.
- Serum prolactin >5000 mU/L is highly suggestive of macroprolactinoma.

Treatment:

- Treat the primary cause and stop the responsible drugs, if any.
- Dopamine agonist drugs (such as bromocriptine, cabergoline and quinagolide) are usually given as a first-line therapy.
- Trans-sphenoidal surgery: May be done in microadenoma. It is also done in macroadenoma; though complete removal may not be possible.
- Radiotherapy: If macroadenoma fails to shrink following dopamine agonist drugs or total surgical removal is not possible.
- In pregnancy, tumour size may be enlarged and may cause headache and visual field defect. In such case, dopamine agonist therapy should be started, if there are symptoms.

Indications of surgery:

- Intolerance to drugs.
- Resistance to drugs.
- Rapid expansion causing mass effect like visual field defect.
- Large cystic macroadenoma.

Cushing Syndrome

Usual instructions are:

- Perform the general examination of this patient.
- Look at the face. What are your findings? What else do you want to examine? (Describe the face as written below. Then mention, 'I want to examine neck (see below), abdomen (striae), proximal myopathy, bony pain due to osteoporosis, BP and urine for sugar test').
- Look at the abdomen. What are your findings? What else do you like to examine? (There are multiple striae and distended abdomen. I want to examine face and other things as above).

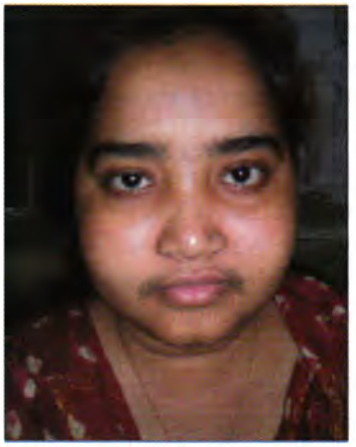
Presentation of a Case

- The patient has moon-like, puffy, plethoric face with acne and hirsutism.
- There is deposition of fat at the root of neck (buffalo hump and increased fat above the supraclavicular fossa).
- The patient is obese. There is truncal obesity with relatively lean and thin limbs (**lemon on a match stick appearance**).
- There are multiple pink or purple striae in abdomen and other parts in skin.
- Skin is thin, with multiple purpura or bruise.
- Proximal myopathy is present.
- There is kyphosis or scoliosis, and tenderness in spine (due to osteoporosis).
- BP is high.

My diagnosis is **Cushing syndrome**.



Cushing syndrome showing plethoric moon face with stria on arm



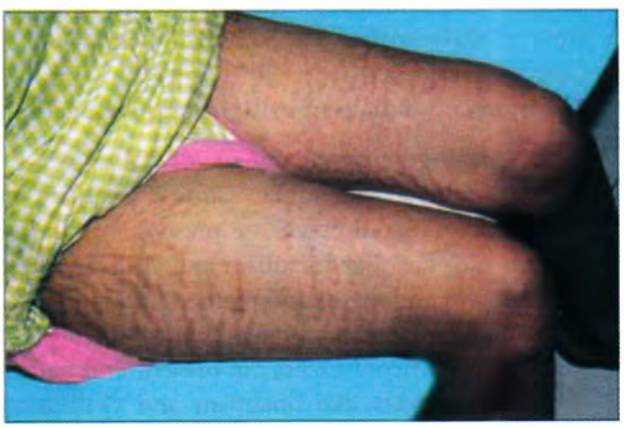
Cushing syndrome (showing hirsutism and plethoric moon face)



Cushing syndrome (buffalo hump—left arrow, supraclavicular fat right arrow, hirsutism)



Cushing syndrome (large breast, striae)



Striae in thigh



Striae in abdomen

Q: What **history** do you like to take? Or ask one **question** to the patient.

A: I want to know about prolonged use of steroid.

Q: What are your **differential diagnoses?**

A: As follows:

- Simple obesity.
- Hypothyroidism.
- Metabolic syndrome.
- Polycystic ovarian syndrome (in early age).

Q: What are the causes of **periorbital oedema?**

A: As follows:

- Nephrotic syndrome.
- Acute glomerulonephritis.
- Myxoedema.
- Angioedema.
- Dermatomyositis.
- Orbital cellulitis.
- Malignant exophthalmos.

Q: What are the causes of **moon face** or puffy face?

A: As follows:

- Cushing syndrome (plethoric moon face, with hirsutism, acne).
- Myxoedema (puffy with baggy eyelids, fall of lateral eyebrows, malar flush).
- Nephrotic syndrome and acute glomerulonephritis (puffy with periorbital oedema).
- Superior vena caval obstruction (engorged and nonpulsatile veins, plethoric face with subconjunctival effusion).
- Angioedema (localized, swollen lip or face).
- Chronic alcoholism (plethoric, puffy face).
- Simple obesity.
- Surgical emphysema. (History of trauma; also swelling is extended up to the neck and chest. There are multiple crepitations on palpation.)

Q: What is the commonest **cause** of Cushing syndrome?
A: Prolonged use of steroid.

Q: Name some diseases where **steroid** is used for prolonged period.
A: Addison disease, SLE, pemphigus vulgaris, dermatomyositis, severe rheumatoid arthritis, hypopituitarism, diffuse parenchymal lung disease (DPLD), etc.

Q: Mention one **absolute indication of steroid therapy.**
A: Pemphigus vulgaris (also Addison disease).

Q: Why **backache** in Cushing syndrome?
A: Osteoporosis (may cause vertebral collapse and kyphosis).

Q: What is the character of **striae** in Cushing syndrome?
A: Striae are pink- or purple-coloured lesions in the skin of abdomen and other parts of body.

Q: What is **Cushing syndrome**? What are the common **features**?
A: It is defined as chronic glucocorticoid excess, whatever is its cause, which leads to constellation of symptoms and signs, commonly:

- Weight gain but weakness.
- Proximal muscular weakness (characterized by difficulty in combing, raising the hands above the head, standing from squatting).
- Hirsutism in female.
- Amenorrhoea or oligomenorrhoea.
- Loss of libido.
- Backache, pathological fracture (due to osteoporosis), collapse of the vertebra with reduction of height.
- Easy bruising, purple abdominal striae.
- Hypertension, DM (30%) or impaired glucose tolerance (IGT).
- Frequent infection, especially fungal infection, slow wound healing.
- Mood disturbance like depression, insomnia, irritability, lethargy.
- On examination: Moon face, buffalo hump, truncal obesity, hirsutism, acne on face, pink striae, growth retardation in children.

Q: What are the **causes** of Cushing syndrome?
A: The common cause is steroid therapy. Other causes:

1. ACTH dependent:
 - Pituitary microadenoma <10 mm called Cushing disease (80%). Common in women.
 - Ectopic ACTH syndrome (oat cell carcinoma of bronchus, bronchial adenoma, bronchial carcinoid and carcinoma of pancreas).
 - ACTH therapy.
2. Non-ACTH dependent:
 - Steroid therapy: The commonest cause (even topical or inhaled steroid for long time in susceptible cases may be responsible).
 - Adrenal adenoma and adrenal carcinoma (common in women).
3. Others: Pseudo-Cushing syndrome (due to alcohol, depression and obesity).

Q: What is **Pseudo-Cushing** syndrome?
A: Cortisol excess due to other illness without involvement of the pituitary adrenal axis is called Pseudo-Cushing syndrome. There is increased urinary excretion of steroid, absent diurnal variation of cortisol and failure of suppression by dexamethasone.

- It may occur in chronic alcoholism, severe depression and in simple obesity. All the features of Cushing syndrome revert to normal after removal of the cause (features in favour of Cushing syndrome are bruise, myopathy and hypertension, all of which are usually absent in Pseudo-Cushing syndrome).
- To differentiate from Cushing syndrome: Insulin-induced hypoglycaemia is helpful. In Cushing syndrome, there is almost no response. But, in Pseudo-Cushing syndrome, there is excess cortisol secretion.

N.B. Remember, if there is history of alcohol intake, advice the patient to stop taking alcohol. Repeat the cortisol or dexamethasone suppression test. It may be normal. Then further test is not recommended.

Q: How to **differentiate clinically** different types of Cushing syndrome?
A: By history, physical examination and investigation:

1. In Cushing syndrome due to adrenal cause:
 - In adrenal adenoma: Clinical features of glucocorticoid excess are present; but androgenic effect like hirsutism and virilization are absent and there is no pigmentation.
 - In adrenal carcinoma: Clinical features of glucocorticoid excess are present and androgenic effects like hirsutism and virilization are rapidly progressive.

2. In ectopic ACTH syndrome: Usually there is short history, excess pigmentation due to high ACTH level, weight loss (rather than obesity) and severe hypokalaemic alkalosis. Hypertension and oedema are more common. Classical features of Cushing syndrome are usually absent.
3. In Cushing disease: There are classic features of Cushing syndrome. If there is pituitary macroadenoma, visual disturbance and features of hypopituitarism may be present. There may be features of raised intracranial pressure like headache.
4. Marked hypokalaemia suggests ectopic ACTH syndrome.
5. History of alcoholism and depression or simple obesity suggests pseudo-Cushing syndrome.

Q: What is the **difference** between Cushing disease and Cushing syndrome?

A: As follows:

- Cushing disease shows increased ACTH from the pituitary gland that stimulates adrenals.
- Cushing syndrome is caused by excess steroid due to any cause.

Q: What are the **causes of death** in Cushing syndrome?

A: As follows:

- Hypertension.
- Myocardial infarction.
- Heart failure.
- Infections.

Q: How to **investigate** Cushing syndrome?

A: Initial tests are done to confirm the diagnosis and further tests are done to find out the cause.

1. Tests to confirm Cushing syndrome:
 - First line screening test:
 - 24-h urinary free cortisol measurement.
 - Overnight dexamethasone suppression test: 1 mg dexamethasone is given orally at 11 pm. Blood sample is taken at 9 am in the next morning to measure serum cortisol. Normally, almost total suppression of cortisol (<100 nmol/L). Failure of suppression indicates Cushing syndrome due to any cause. This test is simple, can be done as an outpatient screening test, but gives some false-positive results.
 - Second-line screening test (if above tests are abnormal):
 - Serum cortisol level (8 am and at 12 midnight): Shows loss of circadian rhythm. Normally, serum cortisol is high in morning and low in midnight (called circadian rhythm).
 - Low-dose dexamethasone suppression test: 0.5 mg 6 hourly for 2 days. Measure serum cortisol at 9 am on days 0 and 2. Failure of suppression of cortisol (<60 nmol/L on second sample) indicates Cushing syndrome due to any cause. Or, 24-h urinary free cortisol <100 nmol/day also excludes Cushing syndrome.
2. Tests to find out the cause (to localize the site of lesion):
 - Serum ACTH:
 - If ACTH is low or undetectable, adrenal cause is likely. Then USG, CT or MRI of abdomen is done to find adrenal tumour. If no mass is seen, then adrenal vein sampling or adrenal scintigraphy should be done.
 - If ACTH is high: Likely cause is pituitary lesion (Cushing disease) or ectopic ACTH syndrome. Now high-dose dexamethasone suppression test or corticotrophin releasing hormone test is done to differentiate between these two.
 - High-dose dexamethasone suppression test: 2 mg 6 hourly for 2 days. Plasma cortisol is measured at 9 am on days 0 and 2. Plasma cortisol on day 2 less than 50% of that in day 0 suggests Cushing disease (in 90% cases). Failure of suppression occurs in ectopic ACTH and adrenal tumour. Urine cortisol <50% of basal suggests Cushing disease and >50% of basal suggests ectopic ACTH syndrome.
 - Corticotropin releasing hormone (CRH) test: 100 µg bovine CRH IV is given. Measure serum ACTH and cortisol for 2 h. It increases in Cushing disease, but no response in ectopic ACTH (peak plasma cortisol >20% and/or ACTH >150% of basal values suggests pituitary disease).
 - If Cushing disease is present: CT or MRI of skull. MRI will show pituitary microadenoma in 70% cases. If no mass is seen, selective catheterization of inferior petrosal sinus to measure ACTH for pituitary lesion.
 - If ectopic ACTH syndrome is the cause: Chest X-ray, CT scan of chest (to see carcinoma of bronchus or bronchial carcinoid).

3. Other tests (to see the effect):
 - Electrolytes (hypokalaemia).
 - Blood sugar.
 - Bone mass density to see osteoporosis.

N.B. Remember the following points:

- Plasma cortisol levels are highly variable. So, random measurement of daytime plasma cortisol level is of no value.
- In pituitary tumour, there is high ACTH and high cortisol.
- In ectopic ACTH syndrome, there is high ACTH and high cortisol.
- In adrenal tumour, there is low or undetectable ACTH and high cortisol.
- Cushing disease and cortisol secreting adrenal tumour are four times common in women than men. But ectopic ACTH syndrome is more in men.

Q: Why **dexamethasone** is used in suppression test? Why **not** other steroids like prednisolone?

A: Because dexamethasone does not cross-react in radioimmunoassay for cortisol. But other steroids can cross-react.

Q: How to **treat** Cushing syndrome?

A: It depends on the cause.

1. Cushing disease:
 - Transphenoidal removal of microadenoma.
 - If surgery is not possible or unsuccessful, bilateral adrenalectomy should be done. Later, the patient may develop Nelson syndrome (see below).
 - If surgery is not possible, sometimes only pituitary irradiation may be given. External irradiation is given. It is slowly effective in 50–60% cases; response in children is better than adults; 80% may be cured.
 - To reduce ACTH production: Bromocriptine or cyproheptadine is rarely effective.
 - Drugs such as metyrapone and ketoconazole may be given.
2. Adrenal tumour:
 - In adrenal adenoma or carcinoma, surgical resection is done (adrenalectomy).
 - In carcinoma, there is chance of recurrence. Then radiotherapy or chemotherapy or adrenolytic drugs like mitotane may be given.
 - Other drugs: Metyrapone or ketoconazole may be used (which inhibits biosynthesis of cortisol).
3. Ectopic ACTH:
 - If possible, the primary lesion should be surgically removed (like bronchial carcinoma or carcinoid). Other treatment of the primary cause like radiotherapy or chemotherapy should be considered.
 - If surgery is not possible, medical therapy as above or bilateral adrenalectomy may be considered.

Q: What is **Nelson syndrome**?

A: Nelson syndrome is characterized by increased pigmentation due to excess ACTH associated with enlarging pituitary tumour, which occurs after bilateral adrenalectomy for Cushing syndrome. It occurs in around 20% cases.

The tumour is locally invasive. It can be prevented by pituitary radiotherapy soon after adrenalectomy.

Treatment: Surgical removal of the tumour. Occasionally radiotherapy (if not given previously).



Nelson syndrome [Bilateral adrenalectomy scar (arrow below); striae, pigmentation (arrow above)]

Addison Disease

Usual instructions are:

- Perform the general examination (emaciation and pigmentation).
- Examine the patient (pigmentation). What else do you want to see?

Proceed as follows:

1. Look for pigmentation (dull, slate-coloured or grey–brown) in the following sites:
 - See the whole body (may be generalized pigmentation).

- Face and neck (exposed parts).
- Mucous membrane of mouth (opposite the molar), lips and conjunctiva.
- Skin crease (palmar crease), knuckles and nipples.
- Pressure points (elbow and knee).
- Recent scar.

2. Check for vitiligo.
3. Monitor BP: Both standing and lying (BP is low and there may be postural hypotension).
4. The patient looks emaciated.

Presentation of a Case

- The patient has generalized pigmentation, more marked in face, neck, mucous membrane of mouth, palmar crease, knuckles, knee and elbow.
- There is also vitiligo (mention where).
- The patient looks emaciated; BP is low and there is also postural hypotension.

My diagnosis is **Addison disease.**

Q: What are the **causes** of pigmentation?
A: See in the chapter "General Examination".

Q: Mention **one investigation** in this patient.
A: Serum cortisol and ACTH level.

Q: What do you **expect** in Addison disease?
A: Low cortisol and high ACTH.

Q: What **investigation** will you do after this finding?
A: Short synacthen test (see below).

Q: What is **Addison disease?**
A: It is the primary adrenocortical insufficiency resulting in glucocorticoid and mineralocorticoid insufficiency. There is destruction of the entire adrenal cortex.

Q: What are the **causes** of Addison disease?
A: As follows:

1. Common causes:
 - Autoimmune mechanism: 80% of the cases (more in female).
 - TB of adrenal gland: 10%.
 - Secondary deposit in adrenals.
 - HIV infection.
 - Bilateral adrenalectomy.
2. Other causes (less common or rare):
 - Amyloidosis.
 - Sarcoidosis.
 - Haemochromatosis.
 - Bilateral adrenal haemorrhage: Following meningococcal septicaemia (Waterhouse–Friedrichsen syndrome) and trauma.
 - Lymphoma.



Pigmentation in crease



Generalized pigmentation



Pigmentation in lips and gum



Pigmentation in palate

Q: What are the **diagnostic criteria** in Addison disease?

A: Triad of:

- Weakness or emaciation (100% cases).
- Pigmentation (90% cases).
- Hypotension (88%).

(Other features: Gastroenteritis in 56%, postural symptoms 12%, salt craving 19%).

Q: What is the **size of heart** in Addison disease?

A: Small heart.

Q: Why does **postural hypotension** occur in Addison disease?

A: It is due to hypovolaemia and sodium loss. Mineralocorticoid deficiency is responsible for hypotension.

Q: What are the **diseases** associated with Addison disease?

A: It is an autoimmune disease; therefore it may be associated with other auto-immune diseases, such as Graves disease, Hashimoto thyroiditis, pernicious anaemia, primary ovarian failure, myasthaenia gravis and type-1 DM, etc.

Q: What are the **presentations** of Addison disease?

A: As follows:

- Chronic adrenocortical insufficiency (weakness, pigmentation, hypotension).
- Addisonian crisis.

• paraneoplastic from Lung Cancer

Q: Why does **vitiligo occur** in Addison disease?

A: It is due to autoimmunity. Vitiligo is present in 10– 20% of the cases.

Q: Why does **pigmentation** occur in Addison disease?

A: Due to excess ACTH that stimulates excess melanin production.

Q: What are the **sites of pigmentation** in Addison disease?

A: As follows:

- May be generalized.
- Exposed parts (face, neck).
- Skin crease (palmar crease) and knuckles.
- Pressure points (elbow, knee).
- Recent scar.

Q: What **investigations** should be done to diagnose Addison disease?

A: As follows:

1. Routine tests:
 - CBC (shows high eosinophil, lymphocyte and ESR). Anaemia may be present, specially associated with pernicious anaemia.
 - Blood glucose (low or lower limit, especially during Addisonian crisis).
 - Electrolytes. (Hyponatraemia and hyperkalaemia. Hyponatraemia is more important than hyperkalaemia. Mild acidosis may be present.)
 - Other tests: Serum renin (increases), aldosterone (low) and serum calcium (may be high).
2. Test to confirm:
 - Plasma ACTH and cortisol measurement is confirmatory (there is high ACTH, >80 ng/L, and low or lower normal cortisol).
 - Short synacthen test should be done. If cortisol level does not rise, it indicates primary or secondary adrenocortical deficiency. Then plasma ACTH should be done. ACTH is high in Addison disease and low or undetectable in ACTH deficiency. If ACTH test is unavailable, long synacthen test can be done to differentiate between primary and secondary adrenocortical deficiency (see below).
3. Tests to find out causes:
 - Chest X-ray (to diagnose tuberculosis).
 - Plain X-ray abdomen (to see adrenal calcification in TB).
 - Adrenal autoantibody.
 - USG or CT scan of adrenals (to look for calcification in TB or malignancy).

4. Other tests:
 - Screening for pernicious anaemia and other autoimmune disorders.
 - Thyroid screening.
 - Other tests according to suspicion of cause (e.g. sarcoidosis, amyloidosis, haemochromatosis, HIV, histoplasmosis, metastatic carcinoma, etc).

Q: How to perform synacthen test?

A: Short synacthen test may be done during anytime of the day, but better at 9 am, nonfasting. It is usually done for:

1. Diagnosing Addison disease.
2. Screening test for ACTH deficiency.

Procedure:

- Short synacthen test: 250 µg ACTH (synacthen or tetracosactrin) IM or IV is given. Serum cortisol is measured at 0 and 30 min. If cortisol rises to >460 nmol/L, it rules out Addison disease. Failure to rise may indicate primary or secondary adrenocortical insufficiency.
- Long synacthen test: 1 mg ACTH IM daily for 3 days. Serum cortisol is measured at 0, 4, 8 and 24 h on each day. Progressive rise of cortisol indicates secondary adrenocortical insufficiency. Failure to rise indicates Addison disease (cortisol remains <700 nmol/L 8 h after last injection).

N.B. Remember the following:

- If the patient is on dexamethasone or betamethasone, it will not interfere with cortisol assay (as these do not cross-react).
- Random cortisol is usually low in Addison disease; but in some cases, it may be within normal or inappropriately low in seriously ill patient. So, random cortisol measurement is of no importance. However, if random cortisol is <100 nmol/L, it is highly suggestive of Addison disease. Also, if the serum cortisol is >460 nmol/L, it rules out Addison disease.
- Single test for diagnosis of Addison disease is the simultaneous measurement of ACTH and serum cortisol level (ACTH is high, cortisol is low).

Q: How to treat Addison disease?

A: As follows:

1. Replacement of hormones:
 - Glucocorticoid:
 - Hydrocortisone: 15 mg in morning (after waking) and 5 mg in afternoon (6 pm). According to some authority, 10 mg after waking up, 5 mg at 12 noon and 5 mg at 6 pm.
 - Or, if hydrocortisone is not available, prednisolone 5 mg on waking in morning and 2.5 mg at 6 pm in afternoon.
 - Mineralocorticoid: Fludrocortisone 0.05–0.1 mg (50–300 µgm) daily.
 - Androgen: Dehydroepiandrosterone (DHEA) 50 mg/day may be given in female. It increases libido and sense of well-being; but complications like acne and hirsutism may occur.
2. Treatment of the cause, e.g. antitubercular therapy in tuberculosis.

General advice to the patient:

- The patient should always carry a bracelet and steroid card, which should contain informations regarding the diagnosis, dose of steroid and doctor's contact address.
- Good nutrition, regular meal, high carbohydrate and sufficient salt.
- The patient should keep ampoules of hydrocortisone at home. If oral therapy is impossible, the patient should take injection by himself, family members or general practitioner (GP).
- The patient should know how to increase steroid replacement dose for intercurrent illness. During intercurrent stress (fever, cold and trauma), the dose should be doubled.

Monitoring of the patient:

- Proper history regarding overall well-being.
- Measurement of BP and weight.
- Serum electrolyte.

N.B. Remember the following points during stress:

1. Intercurrent stress (fever, cold and trauma): Double dose of steroid.
2. During surgery:
 - Minor surgery: Hydrocortisone 100 mg IM or IV premedication.
 - Major surgery: Hydrocortisone 100 mg IM or IV 6 hourly for 24 h; then 50 mg 6 hourly. It should be continued until the patient is capable of taking by mouth.
3. If gastroenteritis: IV or IM hydrocortisone should replace oral therapy.

Q: What is **Addisonian crisis?**

A: It is an acute severe adrenocortical insufficiency characterized by circulatory shock with severe hypotension. It is often precipitated by intercurrent disease, surgery or infection. The patient presents with muscle cramps, nausea, vomiting, diarrhoea, acute abdomen, collapse and unconsciousness. There may be unexplained fever. Laboratory findings include hyponatraemia, hyperkalaemia, and, in some cases, hypoglycaemia and hypercalcaemia.

Causes:

- Sudden withdrawal of steroid (common cause, if patient is on steroid for long time).
- Stress (severe infection and operation).
- Bilateral adrenal haemorrhage (meningococcal septicaemia, injury and anticoagulant).
- Thyroxine therapy in a patient with hypopituitarism without steroid therapy.

Treatment:

- Blood is taken to measure cortisol, glucose and electrolytes.
- Three problems are present: Shortage of salt, sugar and steroid (3S).
- IV fluid, normal saline rapidly (1 L in 30–60 min). Subsequently, several litre of normal saline may be required in 24 h.
- IV 10% glucose.
- IV hydrocortisone 100 mg stat. Then hydrocortisone 100 mg IM 6 hourly, which is continued until the patient is stable and can take by mouth. Then oral steroid is started. Initially hydrocortisone 20 mg 8 hourly, reducing to 20–30 mg in divided doses over a few days (then original replacement therapy should be given).
- Treatment of underlying cause (e.g. infection, adrenal or pituitary pathology, etc).

N.B. Remember the following:

- In severe hyponatraemia (<125 mmol/L), hypertonic saline is unnecessary; plasma Na should not be increased >10 mmol/L/day. This may cause central pontine myelinolysis (osmotic demyelination syndrome).
- During crisis or acute illness, mineralocorticoid such as fludrocortisone is unnecessary, as high dose of steroid provides sufficient mineralocorticoid activity. It can be started later on.
- For hyperkalaemia, volume replacement is sufficient. No extra treatment is usually necessary, but occasionally requires specific therapy.

Q: What drug is **avoided** in acute abdominal pain in Addison disease?

A: Morphine, as patients are more sensitive to this drug.

Q: How to **differentiate** between primary and secondary adrenocortical insufficiency?

A: As follows:

Topic	Primary	Secondary
Site	Primary involvement of adrenal gland	Cause in pituitary or prolonged use of steroid
Pigmentation	Present	Usually pallor
BP	Low	Normal because aldosterone secretion is not dependent on ACTH
Secondary sex character	Normal	Early loss of secondary sex characters. Also, there are features of deficiency of other pituitary hormones.
ACTH	High	Low
Electrolytes	Low Na+, high K+	Usually normal
Autoimmune disease	Autoimmune diseases are associated	Unlikely

Tall Stature

Usual instructions are:

- Perform the general examination.
- Look at the patient (patient looks tall). What else do you want to do?

Proceed as follows:

1. **Appearance:** If tall and obese, it may be Klinefelter syndrome. If tall, lean and thin, it may be Marfan syndrome.



Tall in Marfan syndrome

2. **If Marfan syndrome is suspected**, then see the following:
 - Measure the height of the patient (from crown to heel).
 - Measure the length of arm span.
 - Measure the length of upper segment (pubic symphysis to vertex) and lower segment (pubic symphysis to sole). Normally, lower segment is larger than the upper segment (in adults the ratio is 0.8:1).
 - Also look for arachnodactyly, high-arched palate, eyes (lens dislocation) and heart [aortic regurgitation (AR)].
3. **If Klinefelter syndrome is suspected**, then see the following:
 - Gynaecomastia.
 - Testis (small).
 - Secondary sexual characters (small genitalia, and absence of axillary and pubic hair and beard).
4. **If the above are excluded**:
 - Examine for evidence of thyrotoxicosis.
 - Examine for evidence of gigantism (tall and proportionately large body).
 - Look for anosmia (Kallmann syndrome).
 - Take family history (familial tall stature and constitutional).

In the examination, usual cases of tall stature are:

- Klinefelter syndrome.
- Marfan syndrome.

Q: What are the causes of tall stature?

A: As follows:

1. Constitutional.
2. Genetic (familial).
3. Marfan syndrome.
4. Homocystinuria.
5. Chromosomal abnormalities (Klinefelter syndrome and Kallmann syndrome).
6. Endocrine (gigantism and thyrotoxicosis).
7. Miscellaneous:
 - Cerebral gigantism.
 - Extra Y syndrome (more Y-chromosome, taller but no excess GH).
 - In prepubertal hypogonadism due to any cause: Tall stature is common because of failure of fusion of epiphysis. But, postpubertal hypogonadism is not associated with tall stature because of fusion of epiphysis.

N.B. Most common cause of tall stature: Constitutional, hereditary or early development.

Klinefelter Syndrome

Usual instructions are:

- Look at the patient. What is your diagnosis? What else do you want to see?
- Perform general examination of this patient.

Presentation of the Case

- The patient is tall and obese. There is bilateral gynaecomastia.
- Both testes are small, pea-sized and firm; the penis is also small and there is absence of pubic and axillary hair, and beard.
- The voice is high pitched.

My diagnosis is **Klinefelter syndrome.**

Q: What is Klinefelter syndrome?

A: It is a chromosomal abnormality in which there is an extra X-chromosome associated with hypogonadism (due to small testis). It is characterized by:

- Tall stature (eunuchoid body proportion: Arm span greater than height and leg is more long; lower extremity is greater than upper extremity).
- Obese.
- Gynaecomastia (carcinoma of breast may develop in 20% cases).
- Absence or rudimentary external genitalia (small penis and testis: volume <5 ml).

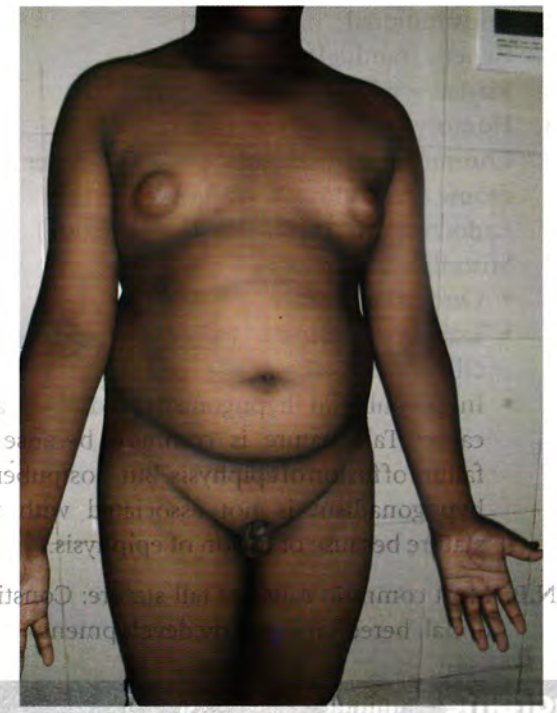
- Absence of secondary sexual characters (axillary, pubic hair and beard).
- High-pitched voice.

N.B. In mosaic, there may be normal puberty. Diagnosis is done during routine investigation for infertility.

Q: What are the usual **presentations** of Klinefelter syndrome?

A: As follows:

- Poor sexual development.
- Infertility.
- Gynaecomastia.
- Small or undescended testis.



Klinefelter syndrome

Q: What is the **abnormality** of the testis?

A: Both testes are small and firm. These show seminiferous tubules dysgenesis. Hyalinization and fibrosis are present within the seminiferous tubules. Leydig cell function is impaired, resulting in hypogonadism. Also, there is azoospermia and high gonadotrophin.

Q: What are the **features** of eunuchoid body proportion?

A: Features are apparent from childhood:

- Tall stature with long leg.
- Hairless face (also sparse body hair).
- High-pitched voice.
- Small and poorly developed external genitalia.
- Immature personality.



Klinefelter syndrome



Small genitalia

Q: Why patient is **tall** in Klinefelter syndrome?

A: Androgen deficiency with lack of epiphyseal closure in puberty.

Q: What **investigations** do you suggest in Klinefelter syndrome?

A: As follows:

- Serum testosterone (low), gonadotrophic hormones (increased FSH and LH).
- Serum oestrogen (increases).
- Azoospermia is universal.
- Chromosomal analysis (two or more X-chromosome, one or more Y-chromosome).

Q: What is the common **karyotype** abnormality?

A: Usually, 47 XXY, which results from nondysjunction during meiosis in one of the parents; may be 46 XY or 47 XXY mosaic.

Q: What are the **associations** in Klinefelter syndrome?

A: The usual associations are:

- DM type-2.
- Low T_4.
- Bronchial asthma.
- Carcinoma of breast in male is more in Klinefelter syndrome.

Q: How to **treat** Klinefelter syndrome?

A: As follows:

- No specific treatment.
- Androgen (testosterone may be used in oral, injection, patch, gel and pellet).
- Plastic surgery for gynaecomastia.
- Life span is usually normal.

Short Stature

Usual instructions are:

- This patient is 25 years old. Look at the patient. What is your diagnosis? What else do you want to see?
- Perform the general examination of this patient, who is 28 years old.

Proceed as follows:

1. History to be taken:
 - Family history (parents and relatives).
 - Pregnancy record (growth retardation and weight at birth, and any congenital disease).
 - Rate of growth.
 - Systemic disease (respiratory, cardiac, GIT and renal).
 - Nutrition (less intake and malabsorption).
 - Age of appearance of secondary sexual characters.
 - Use of steroid during childhood.
 - Psychosocial deprivation.
2. Physical examination:
 - Height and weight chart (if height is below third percentile, it is considered as short stature).
 - Arm span and height (achondroplasia).
 - Short limbs compared to trunk (achondroplasia).
 - Reduction of weight and height (malnutrition and systemic disease).
 - More weight but short height indicates endocrine disease (hypothyroidism, Cushing syndrome), and genetic syndrome (Prader–Willi syndrome, Laurence–Moon–Biedl syndrome).
 - Look for evidence of systemic disease (heart, kidney and respiratory).
 - Others (Turner syndrome, Noonan syndrome and pseudohypoparathyroidism).

Causes of short stature:

1. Constitutional (the commonest cause).
2. Familial or genetic.
3. Physiological growth delay.
4. Chronic systemic disease (heart, kidneys and respiratory).
5. Endocrine diseases:
 - Hypopituitarism.
 - Isolated GH deficiency.
 - Cretinism (hypothyroidism).
 - Cushing syndrome.
 - Pseudohypoparathyroidism.
6. Nutritional (protein energy malnutrition, e.g. kwashiorkor, marasmus, rickets).
7. Chromosomal abnormalities:
 - Turner syndrome.
 - Noonan syndrome (male Turner).
8. Skeletal dysplasia:
 - Short limb and normal trunk (achondroplasia).
 - Short limb and short spine: Mucopolysaccharidoses (Hurler syndrome).
9. Psychosocial deprivation.
10. Others: β-Thalassaemia major, cystic fibrosis, juvenile idiopathic arthritis (JIA).

Features of achondroplasia:

- Short stature.
- Large head. Face is small; nasal bridge is flat.
- Short and broad limbs (both upper and lower). Trunk has normal growth.
- Normal development: Dental, endocrine, sexual, etc.
- Normal intelligence.

It results from defect in the fibroblast growth factor receptor-3 gene. There is decrease in proliferation of the cartilage present in growth plate. It is inherited as autosomal dominant disease.



Twenty-year-old girl with JIA



Achondroplasia



Pseudohypoparathyroidism



Constitutional short stature

Q: How to investigate short stature?

A: After exclusion of systemic disease, proceed as follows:

- Bone age (constitutional delay, hypothyroidism and GH deficiency).
- Lateral skull X-ray (may show calcification).
- Thyroid screening.
- GH assay (better do the stimulation test).
- Other tests according to suspicion of causes.

Diabetes Mellitus

Common short cases selected in any clinical examination related to DM are already described in this book (Chapter 1). Usual cases are:

- Diabetic foot (page 39)
- Leg ulcer (page 36)
- Diabetic amyotrophy (page 41)
- Lipodystrophy of thigh (page 42)
- Necrobiosis lipoidica diabeticorum (page 43)
- Diabetic neuropathy (page 330)
- Diabetic retinopathy (page 445).

In a diabetic patient, examination involves multiple systems of the body. General inspection may give a clue to any underlying cause of DM. Look at the face (e.g. Cushing syndrome and acromegaly, which are the causes of secondary DM). Generalized pigmentation occurs in haemochromatosis called bronze diabetes.

Also, general examination may show any complication (e.g. diabetic foot, nephropathy, neuropathy and so on).

However, there may be other instructions by the examiner, described as follows:

Usual Instruction is (Case No. 1):

- Perform the general examination of this diabetic patient.

Proceed as follows:

1. Look at the patient for:
 - Cachexia (in type-1 DM) or obesity (in type-2 DM)
 - Generalized pigmentation (found in haemochromatosis called bronze diabetes).
 - Kussmaul breathing or air hunger (found in diabetic ketoacidosis).
2. Look at the face for:
 - Signs of Cushing syndrome, thyrotoxicosis or acromegaly, which may cause DM.
 - Ear infection, xanthelasma, corneal arcus, ocular palsy and other obvious cranial nerve palsy (e.g. Bell palsy).
3. Examine the oral cavity for oral candidiasis.
4. Examine the neck for thyromegaly (DM may occur in thyrotoxicosis).
5. Examine the neck and axilla for acanthosis nigricans (associated with insulin resistance).
6. Look for dehydration (in diabetic ketoacidosis) and sweating (in hypoglycaemia) or oedema (diabetic nephropathy).
7. Examine the skin for hypopigmentation (vitiligo may indicate autoimmune cause of DM), diabetic dermopathy, ulcers, infections (boils, carbuncle, cellulitis), necrobiosis lipoidica diabeticorum, fat atrophy or hypertrophy in injection sites, granuloma annulare, hair loss and skin atrophy. Look for fungal infection in nails.
8. Look for any obvious muscle wasting (in thigh called diabetic amyotrophy) or joint deformity (Charcot joint) and Dupuytren contracture or trigger finger. Also in lower limbs, look for calluses, nail change, ankle reflex and foot deformities such as hammer or claw toes.
9. Feel the peripheral pulses (reduced or absent in atherosclerosis), look for fixed heart rate or loss of sinus dysrhythmia (autonomic neuropathy) and auscultate carotid arteries (for bruit in atherosclerosis).
10. BP (lying and standing to see postural hypotension, found in autonomic neuropathy).
11. At the end, examine the urine for sugar, proteinuria and ketone bodies.

Usual Instruction is (Case No. 2):

- Examine the lower or upper limbs of this diabetic patient.

Proceed as follows (lower limbs):

1. Inspection:
 - Necrobiosis lipoidica diabeticorum (central yellow scar with surrounding red margin, found over the shins, due to atrophy of subcutaneous collagen).
 - Ulceration and infection (boils, abscess, gangrene, carbuncle and cellulitis). Look at the sole and between the toes.
 - Diabetic dermopathy (small rounded plaques with raised border over the shins in a linear orientation). Look for any pigmented scars (late diabetic dermopathy).
 - Injection marks on thighs and fat atrophy or hypertrophy.
 - Hair loss and skin atrophy (found in small vessel disease).
 - Muscle wasting (due to neuropathy or diabetic amyotrophy, or as a part of generalized wasting).
 - Examine both knee joints (swollen joints—deformity indicates Charcot joints).
2. Palpation:
 - Temperature (may be cold and blue due to peripheral vascular disease and associated skin atrophy or absent pulses).
 - Pulsation (absent due to peripheral vascular disease or atherosclerosis) and bounding pulse (in neuropathy).
 - Pitting oedema (nephropathy and autonomic neuropathy).
3. Auscultate over femoral artery (for bruit).
4. Perform neurological examination of lower limbs (see page 313).

Usual Instruction is (Case No. 3):

- Examine eyes of this diabetic patient.

Proceed as follows:

- Look for xanthelasma and corneal arcus (occurs in hyperlipidaemia in association with DM).
- Acuity of vision.
- Argyll Robertson pupil.

- Rubeosis iridis (new vessels on the anterior surface of iris).
- Cataract.
- Examine the cranial nerves III, IV and VI (especially the third nerve palsy; if it occurs in DM, it spares the pupil).
- Finally, perform fundoscopic examination for diabetic retinopathy.

Q: What are the causes of **loss of vision** in DM?

A: As follows:

- Diabetic retinopathy.
- Cataract.
- Age-related macular degeneration.
- Retinal vein occlusion.
- Retinal artery occlusion.
- Nonarteritic ischaemic optic neuropathy.
- Glaucoma.

Read the Following Topics in Relation to Diabetes Mellitus

Q: What are the **criteria** for the diagnosis of DM?

A: Criteria for diagnosis of DM are:

- Fasting plasma venous blood sugar level >7.0 mmol/L (or 2-h postprandial blood sugar level >11.1 mmol/L).
- Random blood sugar >11.1 mmol/L.
- During OGTT, >11.1 mmol/L 2 h after 75 g glucose.

N.B. Remember the following points:

- Random means without regard to time since the last meal.
- Fasting means no calorie intake for 8 h at least (not more than 16 h).
- Fasting blood sugar <5.6 mmol/L is normal.
- In symptomatic patient, one abnormal finding is diagnostic of DM.
- In asymptomatic patients, two values are required.
- For OGTT, only fasting glucose and 2 hours after 75 g of glucose are sufficient for diagnosis.
- OGTT should be done only for borderline cases (fasting glucose 6.1–7.0 mmol/L or random glucose 7.8–11.0 mmol/L) and also for the diagnosis of gestational diabetes mellitus (GDM).

Q: What is **impaired glucose tolerance (IGT)**?

A: When fasting glucose is <7 mmol; but during OGTT, 2 h after the glucose load is 7.8–11.0 mmol, it is called IGT. The patient who has IGT is at increased risk of developing frank DM type-2 with time and also macrovascular complications are more (mainly cardiovascular).

Lifestyle modification for type-2 DM and annual check-up for glucose are recommended for this patient. Cardiovascular risk factors should be treated aggressively.

Q: What is **impaired fasting glucose (IFG)**?

A: IFG is defined as the fasting glucose level between 6.1 and 6.9 mmol/L (110–125 mg/dL) according to WHO. However, American Diabetes Association (ADA) defines it as fasting glucose level between 5.6 and 6.9 mmol/L (100–125 mg/dL). These patients are prone to develop frank DM and cardiovascular disease. The patient is advised for weight reduction of about 5–10% of their body weight, regular exercise and follow-up. Usually no drug therapy is recommended.

N.B. Patients with IGT and/or IFG are now regarded as **prediabetics**.

Q: What is **latent diabetes**?

A: It means blood glucose is usually normal, but may be high under certain stressful conditions. Examples are: pregnancy, infection, obesity, stress or drugs like steroid, thiazide diuretics, etc.

Q: What is **potential diabetes**?

A: It means blood sugar usually is normal, but the patient has increased risk of developing DM in future due to genetic reasons like:

- Both parents are diabetic.
- One parent is diabetic and the other has a family history of diabetes.
- Has a diabetic sibling.
- In a twin, if one is diabetic.

Q: What is **brittle diabetes**?

A: Brittle diabetes (or unstable diabetes or labile diabetes) refers to uncontrolled insulin-dependent DM with recurrent, dramatic, large swings in blood glucose levels, often without any apparent reason. This leads to irregular and unpredictable hyperglycaemia, frequently with ketosis, and sometimes serious hypoglycaemia.

Brittle diabetes occurs in 1–2% of diabetics, usually in young (15–30 years) patient with type-1 DM, but may also be found in elderly patient with type-1 or type-2 DM. It often develops after total pancreatectomy. It may be caused by gastrointestinal absorption problems including delayed stomach

emptying (gastroparesis), drug interactions, problems with insulin absorption or hormonal malfunction.

Q: Classify DM aetiologically.

A: Aetiological classification of DM:

1. Type-1 DM:
 - Idiopathic.
 - Immune mediated.
2. Type-2 DM.
3. Gestational DM.
4. Other specific types:
 - Genetic defects of β-cell function.
 - Genetic defects of insulin action.
 - Genetic syndromes such as Down syndrome, Klinefelter syndrome, Turner syndrome and DIDMOAD (*D*iabetes *I*nsipidus, *D*iabetes *M*ellitus, *O*ptic *A*trophy and *D*eafness) syndrome.
 - Pancreatic diseases such as chronic pancreatitis and haemochromatosis.
 - Endocrine diseases such as acromegaly, Cushing syndrome, glucagonoma and thyrotoxicosis.
 - Drug induced (e.g. corticosteroid).
 - Viral infections (e.g. congenital rubella, mumps and Coxsackie virus B).
 - Uncommon form of immune-mediated DM.

Q: What is **gestational diabetes mellitus (GDM)**? How is it **diagnosed**?

A: It is defined as any degree of glucose intolerance with the onset or first recognition during pregnancy. It constitutes 90% of women with pregnancy complicated by diabetes. More than 50% women ultimately develop diabetes in the next 20 years and this is linked with obesity. Mostly they develop type-2 DM.

Oral glucose tolerance test (OGTT) with 75 g of glucose is used as a screening test for gestational diabetes mellitus (GDM) for women between 24 and 28 weeks of gestation. Blood glucose is measured at fasting, 1 and 2 h after glucose load. GDM is diagnosed if blood glucose is:

- fasting >5.1 mmol/L
- after 1 h 10 mmol/L
- after 2 h 8.5 mmol/L.

Q: What are the complications of **foetus** in DM during pregnancy?

A: As follows:

- Teratogenicity (if DM is present in early pregnancy, in the first 6 weeks), there may be cardiac, renal and skeletal malformations, characteristically caudal regression syndrome, neural tube defect.
- Foetal macrosomia (if DM is present in later pregnancy).
- Neonatal hypoglycaemia (as maternal glucose crosses the placenta, but insulin cannot. As a result, fetal islet cells secrete excess insulin, which may cause neonatal hypoglycaemia).
- Increased risk of polycythaemia, hyperbilirubinaemia and hypocalcaemia.
- Hyaline membrane disease.

Q: What is the cause of **macrosomia** in DM?

A: Macrosomia means large or big baby (birth weight >90 percentile for gestational age). It is due to persistent maternal hyperglycaemia leading to foetal hyperglycaemia and prolonged foetal hyperinsulinism. This stimulates excessive somatic growth mediated by insulin-like growth factors (IGFs). Macrosomia affects all organs except the brain.

Q: What are the **complications** of DM?

A: As follows:

A. Acute complications:
 - Hypoglycaemia.
 - Diabetic ketoacidosis.
 - Hyperosmolar nonketotic diabetic coma.
 - Lactic acidosis.
 - Infections: Boils, carbuncle, abscess, cellulitis, tuberculosis.

B. Long-term complications:
 1. Microvascular:
 - Neuropathy: Peripheral neuropathy (sensory, motor or mixed), mononeuritis multiplex, mononeuropathy, autonomic neuropathy.
 - Nephropathy (CKD).
 - Eye complications (retinopathy, cataract).
 - Foot complications (ulcers, gangrene, arthropathy).
 2. Macrovascular:
 - Coronary circulation: Myocardial ischaemia, infarction.
 - Cerebral circulation: Transient ischeamic attack (TIA), cerebrovascular diseases (CVD).
 - Peripheral circulation: Ischaemia, claudication.
 - Foot complications (ulcers, gangrene, arthropathy).

N.B. Diabetes mellitus can cause painless or silent myocardial infarction. Foot complications are due to both macro- and microvascular.

Q: What are the **types of neuropathy** in DM?

A: As follows:

- Sensory neuropathy (common).
- Mixed motor and sensory neuropathy.
- Asymmetrical motor neuropathy (diabetic amyotrophy).
- Autonomic neuropathy.
- Mononeuropathy.
- Mononeuritis multiplex.

Mechanism of neuropathy in DM:

- Axonal degeneration.
- Patchy or segmental demyelination.
- Involvement of intraneural capillaries.

Q: What are the features of **autonomic neuropathy** in DM?

A: In both type-1 and -2 DM, there may be autonomic neuropathy, which involves multiple systems of the body. Features are:

- CVS: Postural hypotension, fixed heart rate, resting tachycardia and, sometimes, sudden death.
- GIT: Gastroparesis and nocturnal diarrhoea, constipation.
- Genitourinary: Urinary incontinence, difficulty in micturition, erectile dysfunction and retrograde ejaculation.
- Sudomotor: Gustatory sweating, nocturnal sweating without hypoglycaemia, hyperhidrosis of upper extremity and anhydrosis of lower extremity, and anhydrosis of foot can cause cracked skin and ulcer.
- Vasomotor: Cold feet due to loss of vasomotor response, dependent oedema due to loss of vasomotor tone and increased vascular permeability.
- Autonomic neuropathy can reduce counterregulatory hormone release, leading to an inability to sense hypoglycaemia appropriately.
- Pupillary: Decreased pupil size, resistance to mydriatic drugs, and delayed or no reflex to light (called pseudo-Argyll Robertson pupil).

Q: What are the causes of **painless myocardial infarction**?

A: As follows:

- DM with autonomic neuropathy.
- Elderly patient with dementia.
- CVD.

Q: What are the causes of **sudden death** in DM?

A: It is more likely due to autonomic neuropathy. Patient usually dies from sudden cardiorespiratory arrest.

Q: What is **insulin resistance syndrome** or **metabolic syndrome** or **syndrome X**?

A: Presence of type-2 DM, central obesity, hypertension and dyslipidaemia (elevated LDL and triglyceride, low HDL) is called metabolic syndrome. Other features are hyperinsulinaemia, microalbuminuria, elevated fibrinogen and plasminogen activator inhibitor 1, plasma uric acid and increased sympathetic activity. The primary defect is insulin resistance. This predisposes to an increased risk of cardiovascular disease.

Q: What **investigations** do you suggest in this case?

A: As follows:

- Urine R/M/E.
- Blood sugar (fasting and 2 h after breakfast)
- HbA_{1C}.
- CBC with ESR.
- Blood urea and serum creatinine.
- Serum lipid profile.
- USG of whole abdomen.
- CXR PA view.
- Plain X-ray abdomen to see pancreatic calcification.
- ECG.

Q: How to diagnose clinically a case of **hypoglycaemic coma** and **hyperglycaemic coma**?

A: Typical features of hypoglycaemic coma are:

- Excessive sweating.
- Tachycardia.
- Tremor.
- Other: Jerks may be brisk, planter—bilaterally extensor.

Typical features of hyperglycaemic coma are:

- Severe dehydration.
- Pulse: Weak, BP—low.
- Air hunger is present: Kussmaul breathing and acetone in the breath are present.
- Others: Reflexes are reduced; planter will be flexor.

Q: What are the **differences** between hypoglycaemic coma and diabetic coma (coma with ketoacidosis)?

A: As follows:

Points	Hypoglycaemic coma	Diabetic coma (DKA)
History	Excess insulin, but no or insufficient food intake following heavy exercise	Too little or no insulin, concurrent infection or digestive disturbance
Onset	Rapid onset, usually after taking insulin. Patient is in good health prior to this.	Slow onset, patient has ill health for several days
Symptoms	Weakness, tremor, sweating, palpitation, hunger, occasional vomiting from depot insulin	Intense thirst, polyuria, dehydration, vomiting, air hunger and abdominal pain
Signs		
• Skin and tongue	• Moist	• Dry
• Eyes	• Normal	• Sunken
• Pulse	• High volume, tachycardia	• Weak
• BP	• Normal or raised	• Low
• Breathing	• Shallow or normal	• Kussmaul breathing
• Acetone smell	• Absent	• Present
• Reflexes	• Brisk	• Diminished
• Plantar response	• Often extensor	• Usually flexor
• Intraocular pressure	• Normal	• Decreased
Urine		
• Ketonuria	• Absent	• Present
• Glycosuria	• Absent	• Present
Blood		
• Glucose	• Hypoglycaemia (<60 mg/dL)	• Hyperglycaemia (>300 mg/dL)
• Bicarbonate	• Normal	• Reduced
• pH	• Normal	• Low
• Acetone	• Normal	• High
Treatment	Oral or IV glucose	Insulin and others
Prognosis	Good	Bad

CHAPTER 7

NEPHROLOGY

"One of the first duties of the physician is to educate the masses not to take medicine"

– Sir William Osler

Usual instructions by the examiner are:

- Examine the abdomen.
- Examine the abdomen and see the relevants.
- Palpate the abdomen. What are your findings?

N.B. For details, see Chapter 4 'Abdomen'.

Once asked to examine the abdomen in relation to nephrology, very likely findings are:

- Unilateral or bilateral renal mass.
- Mass in the right or left iliac fossa (transplanted kidney).
- Abdominal distention due to ascites (as in nephrotic syndrome).

Once a **renal mass** is present, the following relevant findings should be seen:

- General features: Pale, pigmented, puffy face with baggy eyelids, generalized oedema.
- Skin lesion like scabies (may be related to poststreptococcal glomerulonephritis).
- Anaemia [indicates chronic kidney disease (CKD) or plethoric face (indicates secondary polycythaemia in polycystic kidney disease)].
- Blood pressure [hypertension in CKD or acute glomerulonephritis (AGN)].
- Arteriovenous (AV) fistula in the wrist or below the clavicle (haemodialysis).
- Fundoscopy (hypertensive retinopathy).

After finishing the physical examination, examiner may ask, 'do you like to perform any investigation?" Answer with "yes, I want to perform bed side urine examination for albumin (in nephrotic syndrome) and sugar (may be related to diabetic nephropathy)'.

Mass in Flank (Renal)

Usual instruction by the examiner:

- Examine the abdomen.
- Palpate the abdomen.

Presentation of Case (Unilateral Mass): Case No. 1

- There is a mass in right (or left) loin or flank, 10 × 9 cm, round in shape, nontender, surface is smooth or irregular, moves with respiration.
- We can get above the swelling.
- On percussion, there is resonance over it (colonic resonance).

My differential diagnosis is a renal mass, which may be due to (causes of unilateral renal mass):

- Renal cell carcinoma (in elderly) or Wilms tumour (in children).
- Unilateral hydronephrosis or pyonephrosis.
- Hypertrophied single kidney (if nephrectomy of other kidney or congenitally one kidney is absent).
- Renal cyst.
- Polycystic kidney with single palpable kidney (due to asymmetrical enlargement).

N.B. Right kidney may be normally palpable.

Q: Suggest **one investigation.**
A: Ultrasonography.

Q: What **investigations** do you suggest?
A: As follows:

- Ultrasonography (USG) of abdomen.
- Complete blood count (CBC), erythrocyte sedimentation rate (ESR).
- Urine routine and microscopic examination.
- Blood sugar.
- Blood urea, serum creatinine.
- Serum electrolytes.

- Computed tomography scan (CT) or magnetic resonance imaging (MRI).
- Intravenous pyelogram (IVP).

Presentation of Case (Bilateral Mass): Case No. 2

- There are bilateral masses in both right and left flanks; right (or left) is larger, surface is irregular, margin is round or irregular, nontender and freely movable from underlying structure.
- We can get above the swelling.
- On percussion, there is resonance over the mass.

Q: What are the **causes** of bilateral renal mass?

A: As follows:

- Polycystic kidney disease.
- Bilateral hydronephrosis.
- Diabetic nephropathy in early stage.
- Amyloidosis.
- Rarely, bilateral renal cell carcinoma.

Q: What **investigations** do you suggest?

A: As above.

Bilateral Renal Mass (Polycystic Kidney Disease)

Usual instruction by the examiner:

- Examine the abdomen.
- Palpate the abdomen.

Presentation of a Case: See in bilateral renal mass.

Q: What is **polycystic kidney disease** (PKD)?

A: It is an inherited cystic disease of the kidney, and is of two types:

- Adult polycystic kidney disease (APKD), autosomal dominant, usually common one. Males and females are equally affected.
- Infantile polycystic kidney disease (IPKD), autosomal recessive, rare and associated with hepatic fibrosis; fatal in first year due to hepatic or renal failure.

Q: What are the **presentations** of adult PKD?

A: As follows:

- May be asymptomatic, detected mass on routine examination.
- Discomfort, pain or heaviness in the loin.
- Recurrent painless haematuria (due to rupture of cyst in renal pelvis or infection).
- Recurrent urinary tract infection (UTI).
- Acute loin pain or renal colic.
- Features of hypertension (after 20 years of age).
- Features of renal failure.
- Cerebrovascular accident (CVA) (usually subarachnoid haemorrhage, due to rupture of berry aneurysm. Or cerebral haemorrhage as a complication of hypertension).

Q: What are the **other features** of PKD?

A: As follows:

- Cystic liver in 30% cases (common in infantile type), but hepatic dysfunction is rare. There may be cyst in spleen, ovary and pancreas.
- Berry aneurysm in circle of Willis 10% (may rupture causing subarachnoid haemorrhage).
- Polycythaemia (due to increased erythropoietin secretion).
- Renal stone in 10% cases (usually calcium oxalate).
- Renal neoplasm rarely.

Q: What are the causes of **acute pain** in PKD?

A: Pain is due to:

- Acute haemorrhage in the cyst.
- Infection in the cyst.
- Renal stone.
- Renal cell carcinoma, rarely.

Q: If the patient is **unconscious**, what is likely **diagnosis**?

A: Subarachnoid haemorrhage (due to rupture of berry aneurysm). Other causes may be:

- Cerebral haemorrhage as a complication of hypertension.
- Sometimes, hypernatraemia (due to salt-loosing nephropathy).

Q: What are the **causes of death** in PKD?

A: Death may be due to:

- Chronic renal failure (in one-third cases).
- Intracerebral haemorrhage.
- Myocardial infarction.

Q: What **investigations** do you suggest?

A: As follows:

- USG (always mention the first investigation).
- Urine R/E (haematuria) and C/S.

- Full blood count (FBC) (polycythaemia may occur).
- Renal function tests (urea, creatinine).
- Serum electrolytes (some cases salt looser).
- High-resolution CT or MRI.
- Intravenous urograms (IVU).



Polycystic kidney disease

Q: What are the **findings** in IVU in polycystic kidney disease?

A: IVU shows:

- Enlargement of both kidneys.
- Stretched, distorted and elongated pelvicalyceal system (giving rise to **spidery** appearance).

Q: How to **manage** the patient of PKD?

A: As follows:

- Control of hypertension.
- Control of urinary tract infection.
- Plenty of fluid.
- Salt (there may be salt looser) in some cases.
- Large cyst: May be aspirated under ultrasonography guidance. Or, laparoscopic cystectomy may be done.
- Treatment of renal failure: Either dialysis, sometimes renal transplantation.
- Genetic counseling.
- Family screening (for any family member after 20 years of age, USG is done to detect cyst).
- Magnetic resonance (MR) angiography to detect berry aneurysm may be considered in some family members, if anyone of the family members with PKD has history of subarachnoid haemorrhage.

N.B. Remember the following points:

- PKD is always bilateral (may be unilateral, if other kidney is absent).
- PKD is a misnomer; cyst occurs in many other organs (liver, spleen).
- More common in sickle cell disease, cystic fibrosis, Huntington disease.
- May be associated with mitral valve prolapses (25%) causing mitral regurgitation, and aortic regurgitation (rarely severe).
- Colonic diverticulas may occur.
- Abdominal wall hernia.
- Polycystic kidney disease is not premalignant.
- Hypertension is present in 75% cases.
- Usually there is polycythaemia due to high erythropoietin level. There may be anaemia; there is chronic renal failure. (However, haemoglobin level is higher than expected for the degree of renal failure.)

Q: What are the features of **infantile PKD**?

A: It is rare, inherited as autosomal recessive and is associated with cyst in other organs and hepatic fibrosis. It is fatal in the first year of life; death is due to renal failure or hepatic failure.

Q: What are the **cystic diseases** of kidney?

A: As follows:

- Simple cyst, usually congenital.
- Acquired cyst, after dialysis (in chronic renal failure).
- Polycystic kidney disease.
- Medullary sponge kidney, with unknown cause, not genetic. Cyst is confined to the papillary collecting ducts. Age 40–60 years; prognosis good. Usually no hypertension or no renal failure).
- Medullary cystic disease (cyst small in cortical or corticomedullary junction. Renal failure is common; hypertension may occur. Patient usually has polyuria, increased thirst and salt loser).

Unilateral Mass (Renal Cell Carcinoma)

Usual instruction by the examiner:

- Examine the abdomen.
- Palpate the abdomen.

Presentation of a Case: See in unilateral renal mass.

Q: What is **renal cell carcinoma**?

A: Renal cell carcinoma (or hypernephroma) is an adenocarcinoma arising from proximal tubular epithelial cells. It is usually unilateral. But in 10% cases, it may be bilateral.

Renal cell carcinoma is highly vascular, microscopically composed of large cells containing clear cytoplasm. Haemorrhage and necrosis give the cut surface a characteristic mixed golden yellow and red appearance.

In Von Hippel–Lindau syndrome, inherited as autosomal dominant, there may be bilateral renal cyst, renal adenoma and renal cell carcinoma.

Q: How the patient **presents** in renal cell carcinoma?

A: It is common in elderly; males are affected twice more than females. The patient may be asymptomatic. It usually presents with a triad of:

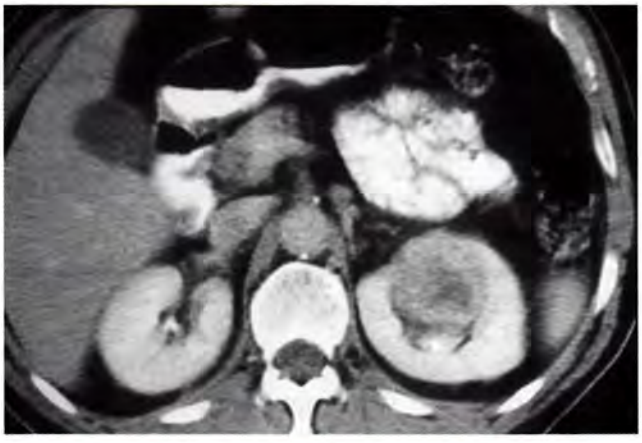
- Painless haematuria (in 50% cases).
- Loin pain or heaviness.
- Palpable mass in loin.

Other features:

- In 20% cases, pyrexia of unknown origin (PUO) may be the only manifestation.
- Features of anaemia and hypertension.
- Malaise, anorexia, weight loss.
- In 5% cases, there may be polycythaemia.
- Some patients may present with features of metastasis. It may spread along the renal vein to inferior vena cava. In renal cell carcinoma of left kidney, it may spread along the left renal vein, which may obstruct the left testicular vein leading to left-sided varicocele. Direct invasion of perinephric tissue is also common. Lymphatic spread occurs to para-aortic lymph node. Also, there may be blood-borne metastasis to any distant organ.



Renal cell carcinoma (right side)



CT scan showing renal cell carcinoma in left kidney

Q: Why **PUO** in renal cell carcinoma?

A: It is due to secretion of pyrogen by tumour.

Q: If the patient has **fever with unilateral renal mass**, what other diagnosis is possible?

A: Renal tuberculosis (or disseminated tuberculosis).

Q: What **investigations** do you suggest?

A: As follows:

- Urine routine and microscopic examination (haematuria may be present).
- Complete blood count (CBC), ESR (anaemia, may be polycythaemia).
- USG.
- CT or MRI (MRI is better for tumour staging).
- IVP.
- USG or CT-guided fine-needle aspiration cytology (FNAC).
- Other investigations for metastasis, e.g. X-ray chest, liver function tests, isotope bone scan, etc.

Q: What may be the **haemoglobin** status of this patient?

A: Usually, there is normocytic and normochromic anaemia. But, there may be polycythaemia in 5% cases.

Q: Why **polycythaemia**?

A: It is due to excess erythropoietin secreted by neoplastic cells.

Q: What peptide **hormones** may be produced by renal cell carcinoma?

A: Erythropoietin, renin, ADH, parathyroid hormone (PTH)-related peptide.

Q: If the patient has **hypercalcaemia**, what may be the cause?

A: It may be due to bony metastasis or secretion of parathormone-like substance.

Q: What **electrolyte** abnormality may occur?

A: Hypokalaemia.

Q: How to **treat** renal cell carcinoma?

A: As follows:

1. Surgery:
 - Radical nephrectomy including perirenal fascial envelope and ipsilateral para-aortic lymph nodes should be done, if possible. This should be performed even if metastasis is present, as it reduces the systemic features and regresses the metastasis.
 - Partial nephrectomy may be done if there are bilateral tumours or the contralateral kidney has poor functional capacity.
2. If surgery is not possible due to high operative or other risk (e.g. single functioning kidney), small tumours may be treated percutaneously by radiofrequency ablation or by tissue-sparing surgery or cryoablation.
3. Medroxy progesterone acetate may be used in metastatic disease.
4. Some benefit may be found with immunotherapy using interferon and interleukin-2.
5. New drugs are:
 - Tyrosine kinase inhibitors, e.g. sorafenib and sunitinib.
 - mTOR (mammalian target of rapamycin) inhibitors, e.g. temsirolimus and everolimus.
 - Bevacizumab, an antibody against vascular endothelial growth factor (VEGF), may slow the progression in metastatic disease.

Prognosis: 5-year survival rate is 60–70%, if tumour is confined to the renal parenchyma; 15–35%, if there is lymph node involvement; and 5%, if there is distant metastasis.

Mass in Left or Right Iliac Fossa (Transplanted Kidney)

Usual instructions are:

- Examine the abdomen.
- Palpate the abdomen.

Presentation of a Case

- There is a mass in right (or left) iliac fossa, 5 × 5 cm, nontender, round in shape, surface is regular, with clear margin.
- There is a laparotomy scar (look for AV fistula in arm).

My diagnosis is **transplanted kidney.**

Q: What are the **indications** of kidney transplantation?

A: End-stage renal disease [when glomerular filtration rate (GFR) is < 5 mL/min].

Q: What are the **causes** of CKD?

A: As follows:

- Glomerular diseases (30–40%), e.g. IgA nephropathy, mesangiocapillary glomerulonephritis (MCGN)
- Diabetes mellitus (20–40%).
- Hypertension (5–20%).
- Obstructive uropathy:
- Chronic pyelonephritis
- Tubulointerstitial diseases (5–10%).
- Systemic inflammatory diseases (5–10%), e.g. systemic lupus erythematosus (SLE), vasculitis.
- Renal artery stenosis (5%).
- Congenital and inherited (5%), e.g. polycystic kidney disease, Alport syndrome.
- Unknown (5–20%).

Q: From where kidney is **collected** for transplantation?

A: It is collected from:

- Matched cadaver donor.
- Relatives who are HLA-identical and ABO-matched.
- Brain-dead person who are on ventilator.

Q: Where the kidney is **placed**?

A: In iliac fossa (either right or left). Donor renal vessels are anastomosed with recipient's external or internal iliac artery and vein.

Q: How do you **diagnose** acute rejection?

A: In the following way:

- Pain in the transplanted area.
- Reduction of urine output.
- Renal area is tender.
- Increased serum urea and creatinine.
- Urine shows plenty of red blood cell (RBC).
- USG shows reduced echogenicity.
- Isotope scan (^{99}TcM or DTPA) shows reduced uptake.
- Graft biopsy may be required.

Q: How to **manage** after rejection?

A: Short course of very-high-dose steroid is given. Other therapies, namely antilymphocyte antibody or plasma exchange, are used in resistant case.

Q: Is there any **bad effect** of repeated blood transfusion before kidney transplantation?

A: Repeated transfusion should be avoided as it carries a risk of HLA sensitization. But pretreatment with multiple transfusions from donor tends to increase graft survival (in contrast to bone marrow transplantation).

Q: What is **CKD** and what is **ESRD**?

A: As follows:

- Chronic kidney disease (CKD) is the irreversible deterioration of renal function classically developing over a period of years. In CKD, glomerular filtration rate (GFR) >10 mL/min, medical treatment is still possible to maintain renal function.
- End-stage renal disease or failure (ESRD) is a stage when renal replacement therapy is compulsory by either dialysis or renal transplantation, without which death is likely. Here GFR <5 mL/min and medical treatment cannot maintain renal function.

Q: What are the **contraindications** of renal transplantation?

A: As follows:

1. **Absolute:**
 - Active malignancy: A period of at least 2 years of complete remission is recommended for most tumours.
 - Active vasculitis or recent anti-GBM (anti-glomerular basement membrane) disease.
 - Severe heart disease or any severe comorbid condition.
 - Severe occlusive aortoiliac vascular disease.
2. **Relative:**
 - Age: While practice varies, transplants are not routinely offered to very young children (<1 year) or older people (>75 years).
 - High risk of disease recurrence in the transplant kidney.
 - Disease of the lower urinary tract: In patients with impaired bladder function, stricture urethra. (An ileal conduit may be considered.)
 - Significant comorbidity.

Q: What drugs are used to **prevent rejection** (or management after transplantation)?

A: Usually a combination of:

- Prednisolone.
- Cyclosporine or tacrolimus.
- Azathioprine or mycophenolate mofetil/sirolimus or everolimus.

Q: What are the **complications of immunosuppression?**

A: As follows:

- Infection (see below).
- Malignancy (see below).

Q: What are the **complications** after renal transplantation?

A: As follows:

- Acute rejection characterized by rising of creatinine, fever, loin pain, hypertension, swelling of the graft. Urine shows protein, lymphocyte, and renal tubular cells. Occurs in 10–30% cases within 6 months. Graft biopsy shows immune cell infiltrate and tubular damage. Treatment: High-dose methylprednisolone; in resistant cases antithymocyte globulin (ATG), antilymphocyte globulin (ALG) or OKT3 may be used.
- Chronic rejection: Usually occurs after 6 months. The patient presents with gradual rise of creatinine and proteinuria. Graft biopsy shows vascular change, fibrosis and tubular atrophy. It is not responsive to increased immunosuppression.
- Infection: Cytomegalovirus (CMV), *Pneumocystis jiroveci*, oral candidiasis, polioma virus. Bacterial infection is common in first few months.
- Complication of immunosuppressive drugs including steroid.
- Acute tubular necrosis (ATN): It is the commonest cause of cadaveric graft dysfunction (40–50%). It is associated with a worse long-term outcome and increases the risk of graft rejection.
- Technical failures: Occlusion or stenosis of the arterial anastomosis, occlusion of the venous anastomosis and urinary leaks.
- Post-transplantation lymphoproliferative disorder: Epstein–Barr virus (EBV)-associated malignancies (such as lymphoma) are common in patients who receive biological agents and in children.
- Chronic allograft nephropathy: Most common cause of late graft failure.
- Malignancy: Skin tumour (including basal and squamous cell carcinoma), renal, cervical and vaginal.
- Hypertension.
- Atherosclerosis.
- Recurrence of renal disease.

Complication of renal transplantation (Remember the formula, '**TROPICAL**'):

- **T**—Thrombosis of graft kidney artery and vein.
- **R**—Rejection of graft kidney.

- O—Obstruction of graft ureter with perinephrichaematoma, seroma, urinoma, or lymphocoele.
- P—Primary disease recurrence. The most common recurrence is MCGN type-II (80–100%).
- I—Infection: Bacterial [any, tuberculosis (TB)], Viral (CMV, chicken pox, polioma virus), fungal, *Cryptococcus neoformans*), Parasite (*Pneumocystis jiroveci*, isospora, Cyclosporidium, Microspora, Giardia).
- C—Cyclosporine toxicity and other immunosuppressive drug toxicities.
- A—Acute tubular necrosis.
- L—Leakage of graft ureter due to error or ischaemia.

Prognosis after kidney transplantation:

Survival in transplant from living donor:

- 1-year survival 85–90%.
- 3-year survival 70–75%.
- 5-year survival 60–65%.
- 10-year survival 50–55%.

Survival in transplant from cadaver donor:

- 96% patient survival and 92% graft survival at 1 year.
- 87% patient survival and 82% graft survival at 5 year.

Nephrotic Syndrome

Instructions by the examiner:

- Look at the face of the patient.
- Do the general examination.

Presentation of a Case

- The patient is grossly oedematous.
- The face is puffy with baggy eyelids.
- Pitting oedema is present.

My diagnosis is **nephrotic syndrome** (NS).

Q: What are your **differential diagnoses?**

A: As follows:

- Acute glomerulonephritis.
- Congestive cardiac failure.
- Cirrhosis of the liver.
- Hypoproteinaemia due to malnutrition or malabsorption.



Nephrotic syndrome



Puffy face with baggy eyelids in nephrotic syndrome



Ascites and oedema in nephrotic syndrome

Q: What **history** would you like to take in NS?

A: As follows:

- Diabetes mellitus.
- Malignancy (lymphoma, leukaemia).
- Drugs, e.g. Captopril, NSAIDs, penicillamine, gold.
- Skin rash, arthritis, arthralgia, alopecia (SLE).

- History of other diseases like malaria, leprosy, syphilis, hepatitis B virus (HBV), hepatitis C virus (HCV), amyloidosis, vasculitis.
- Family history of sickle cell disease, Alport syndrome, nail patella syndrome.

Q: What bedside test do you like to do?

A: Bedside urine examination (shows massive proteinuria).

Q: What investigations should be done in nephritic syndrome?

A: As follows:

1. Urine R/E: Shows gross proteinuria. Red cells and red cell casts are absent. (Also look for urine sugar to exclude diabetic nephropathy.)
2. 24-h urinary total protein (more than 3.5 g/24 h is suggestive of nephritic syndrome).
3. Serum total protein, serum albumin and A:G ratio (hypoalbuminaemia).
4. Serum lipid profile [high cholesterol and high triglycerides (TG) may be present].
5. Blood sugar, blood urea, serum creatinine, serum electrolytes should be done.
6. USG of the whole abdomen to look for renal pathology.
7. To find out causes:
 - Blood sugar (to exclude diabetic nephropathy).
 - Chest X-ray (to exclude bronchial carcinoma, lymphoma; also to see bilateral pleural effusion, pericardial effusion).
 - Antinuclear antibody (ANA), anti-double-stranded DNA (anti-dsDNA) (if the history is suggestive of SLE).
 - Perinuclear antineutrophil cytoplasmic antibodies (P-ANCA) and cytoplasmic anti-neutrophil cytoplasmic antibodies (C-ANCA) (if the history is suggestive of vasculitis).
 - Hepatitis B surface antigen (HBsAg) and anti-HCV screening.
 - Complement C3 and C4.
 - Renal biopsy [to see the type of glomerulonephritis (GN), whether minimal, membranous or membranoproliferative]. (This will guide for diagnosis, therapy and prognosis.)

Q: What is nephrotic syndrome? What are the causes?

A: Nephrotic syndrome is characterized by generalized oedema, massive proteinuria and hypoalbuminaemia (with or without hyperlipidaemia). Causes are:

1. Primary renal disease: All glomerulonephritides (80%):
 - Minimal-change glomerular disease (commonest in children).
 - Membranous GN (commonest in adult).
 - Mesangiocapillary and proliferative glomerulonephritis.
 - Focal and segmental glomerulosclerosis.
 - IgA nephropathy.
2. Secondary to other disease:
 - Diabetic nephropathy.
 - Collagen disease, mainly SLE; also rheumatoid arthritis (by amyloidosis).
 - Amyloidosis.
 - Drugs: Penicillamine (common), captopril, gold, mercury.
 - Neoplastic: Carcinoma (bronchial carcinoma), lymphoma.
 - Infection: Malaria (quartan malaria), bacterial endocarditis, HBV, HCV, human immunodeficiency virus (HIV), secondary syphilis, leprosy.
 - Allergies: Bee stings, snake bite, antisnake venom, pollens.

Q: What is the commonest cause of nephrotic syndrome in children and adult?

A: Commonest cause in children is minimal-change glomerulonephritis; and the commonest cause in adult is membranous glomerulonephritis.

Q: What are the lipid abnormalities in NS? What are the mechanisms?

A: Lipid abnormalities are:

- Hypercholesterolaemia.
- High low-density lipoprotein (LDL), very-low-density lipoprotein (VLDL) and intermediate-density lipoprotein (IDL).
- HDL shows no change, or it may be low.

The mechanisms are:

- Increased synthesis of lipoproteins by the liver, secondary to hypoalbuminaemia.
- Reduced clearance of triglyceride-bearing lipoprotein (chylomicron and VLDL) in direct response to albuminuria.

As a result, there is high rate of atherosclerosis.

Q: What are the mechanisms of proteinuria?

A: There is increased permeability of the glomerular capillary wall due to:

- Reduction of fixed negatively charged protein molecules in glomerular capillary wall, which repels negatively charged protein molecules and allows proteins to pass through the pores.

- Damage to the glomerular basement membrane that leads to increase in the size and number of pores allowing passage of larger molecules.

Q: Why oedema in NS?

A: Previously it was thought that reduction of albumin causes low plasma oncotic pressure leading to oedema. But recent view is that oncotic pressure is not changed in NS; oedema is due to sodium retention in the extracellular compartment. Also, there is change in molecular barrier, which causes oedema.

Q: What is the blood pressure in NS?

A: Usually blood pressure is normal, even low. If there is hypertension, usually it is secondary to underlying diseases like SLE with renal involvement, polyarteritis nodosa, diabetic nephropathy or terminal stage of nephrotic syndrome.

Q: How to treat nephrotic syndrome?

A: As follows:

1. Fluid restriction: Depending on previous day's output and patient's oedema status (average – 500–1000 mL/day).
2. Salt restriction.
3. High-protein diet (2 g/kg/day). In severe case, intravenous salt-poor albumin may be given in diuretic resistant patients and in those with oliguria and uraemia in the absence of severe glomerular damage, e.g. in minimal change nephropathy. It helps in diuresis. Protein intake should be restricted in patient with impaired renal function.
4. Diuretics: Loop diuretics (frusemide, bumetanide). Potassium-sparing diuretics (spironolactone) may be added.
5. ACE inhibitor or angiotensin II receptor antagonist is used in all types of GN (for their antiproteinuric properties. These drugs reduce proteinuria by lowering glomerular capillary filtration pressure).
6. In case of minimal-change disease:
 - Prednisolone: 60 mg/m^2 body surface area (maximum 80 mg/day) is given for 4–6 weeks, followed by 40 mg/m^2 every alternate day for a further 4–6 weeks. More than 95% responds (in children). Alternately, prednisolone 1 mg/kg/day up to response (urine protein free) or 3 months followed by tapering the dose in next 3 months.
 - If there is relapse after withdrawal of steroid, it should be given again with gradual withdrawal. Some patients may require low-dose maintenance dose (5–10 mg/day) for 3–6 months.
 - If there is frequent relapse or there is a need for high-dose steroid or incomplete response to steroid: Cyclophosphamide (2.0 mg/kg/day for 8–12 weeks) and mycophenolate mofetil with low-dose steroid should be given.
7. In membranous glomerulopathy, the following treatment may be given:
 - Inj. methylprednisolone 500–1000 mg intravenous (IV) for 3 days followed by oral prednisolone 0.5 mg/kg/day for 27 days in first, third and fifth months and tab. cyclophosphamide 2 mg/kg/day or chlorambucil 0.2 mg/kg/day for 30 days in second, fourth and sixth months.
 - Chlorambucil (0.2 mg/kg/day in months 2, 4 and 6 alternating with oral prednisolone 0.4 mg/kg/day in months 1, 3 and 5) or cyclophosphamide (1.5–2.5 mg/kg/day for 6–12 months with 1 mg/kg/day of oral prednisolone on alternate days for the first 2 months) are equally effective. However, this treatment is reserved for patients with severe or prolonged nephrosis (proteinuria >6 g/day for >6 months), or renal insufficiency and hypertension.
 - Cyclosporine and mycophenolate mofetil with oral steroid may be used.
 - Anti-CD20 antibodies (rituximab) have been shown to improve renal function, reduce proteinuria and increase the serum albumin.
 - Oral high-dose corticosteroid and azathioprine are ineffective.
8. Focal and segmental glomerulosclerosis:
 - Symptomatic and supportive treatment.
 - Steroid is effective in 40% cases. Tab. prednisolone 1 mg/kg/day for 3 months and then tapered. Total duration of treatment is at least about 6 months to 1 year. Most cases progress to renal failure.
 - If no response: Mycophenolate mofetil 1–2 g/day or cyclosporine 5–6 mg/kg/day for 3 months and then tapered and maintained up to 15 months.
 - Tacrolimus 0.05 mg/kg/day may be tried (occasionally effective).
 - Renal transplantation can be done in renal failure, but may relapse after transplantation.
9. Mesangiocapillary or membranoproliferative GN:
 - Only symptomatic and supportive treatment.
 - No specific treatment.
 - Aspirin may be given.

10. Treatment of complication:
 - If infection: Antibiotic is given. Pneumococcal vaccine is recommended.
 - Venous thrombosis: To prevent, prolong bed rest should be avoided. Prophylactic heparin if immobile (enoxaparin may be given), followed by oral anticoagulant.
 - For hyperlipidaemia: Statin may be added.
11. Treatment of underlying cause, if any.

Q: What is the **prognosis** in NS?

A: It depends on the type of NS.

- Prognosis of minimal-change disease in children is excellent. Remission and relapse may occur most commonly in children and less in adult. CKD does not occur.
- In membranous nephropathy, one-third may remit spontaneously, one-third remains in nephrotic syndrome and one-third shows progressive loss of renal function.
- In focal segmental glomerulosclerosis (FSGS) and mesangiocapillary GN: Prognosis is bad.
- IgA nephropathy: Course of the disease is indolent. ESRD occurs in 20 years.

Q: What are the **complications** of nephrotic syndrome?

A: As follows:

- Hypercoagulability leading to venous thrombosis [especially renal vein thrombosis, also deep vein thrombosis (DVT)] and pulmonary embolism.
- Infections such as pneumococcal infection (may cause peritonitis and septicaemia), cellulitis, streptococcal infection, etc. due to loss of immunoglobulin (IgG deficiency) complements.
- Hyperlipidaemia leading to atherosclerosis.
- Oliguric renal failure.
- May cause bilateral pleural effusion, pericardial effusion.
- Loss of thyroxin-binding globulin that causes low FT_3 and FT_4, which leads to hypothyroidism.
- Loss of transferrin and iron, resulting in iron-deficiency anaemia.
- Loss of vitamin D-binding protein, leading to osteomalacia.

Q: What are the **mechanisms of renal vein thrombosis** in nephrotic syndrome?

A: Mechanisms are as follows:

1. In nephrotic syndrome, there is hypercoagulable state due to:
 - Loss of inhibitors of coagulation in urine such as antithrombin III, protein C and S, and also loss of fibrinolytic factor (plasminogen).
 - Increased synthesis of clotting factors: Factors V, VIII and fibrinogen.
 - Other factors: Thrombocytosis and over diuresis resulting in dehydration, reduced renal blood flow and increased viscosity, prolonged bed-ridden condition.
2. Also, there is hyperlipidaemia, commonly high LDL, VLDL, cholesterol and triglyceride. So, there is more atherosclerosis.

These predispose to increased venous thrombosis that occurs especially in renal vein.

In nephrotic syndrome, if there is loin pain, haematuria and deterioration of renal function, it is highly suggestive of renal vein thrombosis. It is more common in membranous nephropathy, mesangiocapillary glomerulonephritis and amyloidosis.

To diagnose renal vein thrombosis, Doppler ultrasound, CT or MRI, sometimes renal angiogram (venous phase) may be done.

Treatment: Anticoagulant heparin for 5–7 days; then warfarin for 3–6 month.

Read the Following Topics in Relation to Nephrology

Types of haematuria:

- Initial haematuria: Presence of blood at the beginning of micturition, usually due to penile urethral cause.
- Terminal haematuria: Presence of blood at the end of micturition, usually due to bladder neck or prostatic urethral cause.
- Total haematuria: Presence of blood throughout micturition, usually due to bladder or urinary tract disease or blood dyscrasia or excess anticoagulant.

Urinary incontinence: It means urine leaks involuntarily. It is of four types:

- Stress incontinence: Loss of urine with activity such as coughing, sneezing, lifting any object, exercise, etc.
- Urge incontinence: Uncontrolled loss of urine preceded by strong urge to void urine. It is due to inflammatory condition or neurogenic bladder.
- Overflow incontinence: Chronic urinary retention associated with this condition.
- Total incontinence: Patient loses urine at any time and at any position due to loss of sphincter efficacy.

Causes of red or dark urine:

- Haematuria (red).
- Haemoglobinuria (dark).
- Myoglobinuria (in rhabdomyolysis).
- Food dye (beet root).
- Drugs: Rifampicin (orange), L-dopa (dark on standing), phenolphthalein (pink) and senna (orange).
- Acute intermittent porphyria (urine is dark, if kept for long time).
- Alkaptonuria (urine becomes black, if kept for long time).

Causes of painless haematuria:

- Renal cell carcinoma.
- PKD.
- Papilloma of urinary bladder.
- Schistosomiasis.
- Benign hypertrophy of prostate.
- Bleeding disorder.
- Heparin, antiplatelet-drug therapy.

Causes of sterile pyuria (urine shows pus cells but is negative on culture):

- Renal tuberculosis.
- Nongonococcal urethritis (Chlamydia, ureaplasma, etc.).
- Schistosomiasis.
- Tubulointerstitial nephritis.
- Papillary necrosis.
- Polycystic kidney.
- Haemorrhagic cystitis (due to cyclophosphamide).
- Inadequately treated UTI.
- Prostatitis.

Q: How to **differentiate** between haematuria and haemoglobinuria?

A: As follows:

Points	Haematuria	Haemoglobinuria
Urine	Red	Dark
Microscopy	RBC present	RBC absent

CHAPTER 8

NEUROLOGY

"The man who confesses his ignorance shows it once, he who tries to conceal it shows many times"

– A Japanese Proverb

Introduction

Neurological cases are the most feared in the examination. However, these cases are probably the most straightforward in terms of diagnosis and defining the site of lesion. To attain efficiency and skillfulness, a good deal of practice is required that will suffice to score highly.

Candidates are expected to know: **'What is the lesion? What is the site of lesion? What is the cause of lesion'?** The signs need to be elicited carefully for exact anatomical localization of any lesion.

Candidates are usually asked:

- Perform the neurological examination of lower limbs (or upper limbs).
- Look at the leg. What is your finding? (wasting, fasciculation or pes cavus).
- Examine the hands (wasting or claw hands).
- Talk to the patient (dysarthria, dysphasia or hoarse voice).
- Look at the patient. What is your diagnosis? (Parkinsonian face or involuntary movement, e.g. tremor, chorea.)
- Examine the cranial nerves or examine the facial nerve.

Occasionally, examiner may ask, **'Examine the legs or lower limbs'**.

One must remember that there may be **nonneurological** cases. Candidates often mistakenly perform the neurological examination only. Hence, never forget the nonneurological cases and examine properly keeping these in mind.

Nonneurological cases may be (look very carefully and diagnosis may be obvious):

- Swelling of knee joints (arthritis or effusion).
- Erythema nodosum.
- Pretibial myxoedema.
- Systemic sclerosis.
- Diabetic foot.
- Unilateral or bilateral leg swelling.
- Vasculitis.
- Necrobiosis lipoidica diabeticorum.
- Bowing tibias (rickets or Paget disease or congenital anomaly).

Even if asked to perform neurological examination, quickly look carefully. After good visual survey, if nothing is obvious, proceed with the neurological examination.

Neurological Examination of Lower Limb

Most likely cases in the examination are:

- Spastic paraplegia or flaccid paraplegia.
- Peripheral neuropathy.
- Friedreich ataxia.
- Motor neuron disease (MND).
- Old poliomyelitis.

Proceed as follows:

Introduce yourself and ensure that lower limbs are well exposed (with permission). The patient should be lying in supine position.

N.B. If urinary catheter is present, it indicates spinal cord compression or disease, mostly multiple sclerosis (MS).

Inspection:

- Wasting (mention the location—right or left or both or thigh or leg).
- Skin change (shiny, pigmented, rough, ulceration, hair loss and gangrene). See the tip of the toes including sole.
- One leg is smaller than the other (old poliomyelitis).

- Pes cavus (right or left or both feet).
- Fasciculation (if not visible, tap the muscle with your fingers).
- Any swelling in calf muscles (pseudohypertrophy of calf muscles).
- Joint abnormality (deformity or swelling, the signs of inflammation).

Palpation:

1. Bulk of the muscles (measure with tape from a particular point):
 - Unilateral wasting (old poliomyelitis).
 - Generalized wasting [MND, polyneuropathy, lower motor neuron (LMN) lesion].
 - Isolated anterior wasting in thigh (diabetic amyotrophy).
 - Wasting in the leg that stops suddenly at a certain level (Charcot-Marie-Tooth disease).
2. Tone: Tell the patient, 'Keep your limbs relaxed':
 - Lift the leg and allow it to fall.
 - Palpate the muscle and perform side-to-side movement of the limb.
 - Lastly, passive movement of the limb (in irregular fashion—flexion and extension).
3. Test for clonus (ankle and patella).
4. Muscle power (against resistance): If any weakness, mention **grading of weakness.** To test, ask the patient to follow your instructions as follows (press by your hand):
 - Hip flexion: 'Raise your leg straight; do not let me push it down'. (Prime mover is iliopsoas—**L1** and **L2**.)
 - Hip extension: 'Push your leg down; do not let me pull it up'. (Prime mover is glutei muscles—**L4** and **L5**.)
 - Hip adduction: 'Push your thighs inwards; do not let me move them apart'. (Prime movers are adductors of thigh, such as adductor longus, brevis and magnus—**L2, L3** and **L4**.)
 - Hip abduction: 'Push your thigh outwards. Do not let me push them inward'. (Prime mover—gluteus medius and minimus, sartorius and tensor fasciae latae—**L4, L5** and **S1**.)
 - Knee flexion: 'Bend your knees; do not let me straighten them'. (Prime mover is hamstrings such as biceps femoris, semimembranosus and semitendinosus—**L5, S1** and **S2**.)
 - Knee extension: 'Straighten your knees; do not let me stop doing it'. (Prime mover is quadriceps femoris—**L3** and **L4**.)
 - Plantar flexion of ankle: 'Push your foot downwards against my hand'. (Prime mover is gastrocnemius, plantaris and soleus—**S1** and **S2**.)
 - Dorsiflexion of ankle: 'Push your foot upwards against my hand'. (Prime movers are tibialis anterior, extensor digitorum longus and extensor hallucis longus—**L4** and **L5**.)
 - Inversion of foot: 'Push your foot inwards against my hand'. (Prime movers are tibialis anterior and posterior—**L5** and **S1**.)
 - Eversion of foot: 'Push your foot outwards against my hand'. (Prime movers are peroneus longus and brevis—**L5** and **S1**.)
 - Extension of great toe: 'Push your great toe upwards and do not let me push it down'. (Prime mover is extensor hallucis longus—**L5**.)
5. Reflexes:
 - Knee (**L3** and **L4**).
 - Ankle (**S1** and **S2**).
 - Plantar (**L5, S1** and **S2**): Mention to the patient, 'I am going to tickle the bottom of your foot', with an orange stick at the outer portion of the sole. Report according to your finding, 'Plantar is extensor or flexor or equivocal'.

 N.B. Remember the following points:
 - If reflexes are absent, **never forget** to do reinforcement. Ask the patient to pull his or her clasped hands outwards (Jendrassik manoeuvre), or clench the teeth and see the reflex.
 - Examine for **Oppenheim** sign (by pressing heavily the shin along the inner border of tibia going down) and **Gordon** sign (by squeezing the Achilles tendon). If these signs are positive, there will be extensor plantar response (indicates extensive pyramidal lesion).
6. Superficial reflexes:
 - Abdominal reflex (**T6–T11**): Elicited by lightly stroking the abdominal wall diagonally towards umbilicus in each of the four quadrants of abdomen. If positive, reflex contraction of abdominal wall occurs. Absent in upper motor neuron (UMN) lesion. Early loss in MS.
 - Cremasteric reflex (**L1–L2**): Stroke the inner part of thigh in downward direction. Normally, contraction of cremasteric muscles pulls up the scrotum and testis on the side stroked.
7. Coordination (Explain and show it to the patient.):
 - Heel-shin test: 'Please raise your leg, put your heel upon the knee of other leg and run it smoothly along the shin'. (Repeat the same for other leg.)
 - Foot taping test: Keep your hand at a little distance from ball of patient's foot and ask the patient to tap it rapidly on your hand (dysdiadochokinesis).

8. Sensory test: Explain to the patient with light touch by cotton-wool in normal area such as forehead. Ask the patient 'Can you feel it'? Now touch the leg or foot. Ask the patient, 'Can you feel it'? If no, continue to touch above, until the patient can feel to find out the level of sensory loss.
 - Light touch (cotton-wool).
 - Pin prick.
 - Vibration sense: Always explain the patient first, should be tested on medial malleolus; if impaired, it may also be tested in knee and anterior superior iliac spine.
 - Position sense (in great toe; always explain this to the patient.)

 Perform the test according to the nerve distribution
 - Outer thigh L2 (upper thigh).
 - Inner thigh L3 (also around knee).
 - Outer leg L5 (up to medial foot).
 - Inner leg L4.
 - Medial foot L5.
 - Lateral foot S1.
9. Gait:
 - Ask the patient to walk, look for any abnormalities and also ask to turn quickly (in Parkinsonism, unable to turn quickly).
 - Ask the patient to walk heel-to-toe (to exclude midline cerebellar lesion—ataxia).
 - Ask the patient to walk on toes (S1 lesion will make it impossible).
 - Ask the patient to walk on heel (L4 and L5 lesion will make it impossible).
10. Test for Rombergism (Ask the patient to stand with legs together and close the eyes. In positive case, the patient tends to sway or fall. Be careful to protect the patient from falling.). If positive, indicates sensory ataxia [due to subacute combined degeneration (SCD) and tabes dorsalis].
11. Finally, look at the spine to see any deformity, scar, gibbus and local tenderness.

Read the following topics carefully.

Grading of muscular weakness, Medical Research Council (MRC) criteria

- **Grade 0:** Complete paralysis.
- **Grade 1:** A flicker of contraction only.
- **Grade 2:** Power detectable, when gravity is excluded by postural adjustment.
- **Grade 3:** Limb can be held against gravity, but not against examiner's resistance.
- **Grade 4:** There is some degree of weakness.
- **Grade 5:** Normal power.

Signs of upper motor neuron (UMN) lesion

- Weakness or paralysis.
- Increased tone (hypertonia, spastic, may be clasp knife).
- Exaggerated tendon reflex, may be clonus and absent abdominal reflex.
- Plantar response: Extensor.
- No wasting (occasionally due to disuse).
- Normal electrical excitability of muscles.
- Upper limb drift: Present (see below).

Q: What are the sites of UMN lesion?

A: In the:
- Cerebral cortex
- Internal capsule
- Brainstem
- Descending tracts up to anterior horn cells of spinal cord.

Signs of LMN lesion

- Weakness or paralysis (flaccid).
- Hypotonia.
- Loss of all reflexes
- Wasting of involved muscles.
- Fasciculation of affected muscles.
- Plantar: Normal or absent.

Q: What are the sites of LMN lesion?

A: In the motor pathway from anterior horn cells (or cranial nerve nucleus) via peripheral nerve to motor end plate.

Signs of extrapyramidal lesion

- Rigidity (leadpipe or cogwheel).
- Hypokinesia or bradykinesia (poverty of movement) or akinesia (no movement).
- Involuntary movements (tremor, chorea, athetosis, dystonia and hemiballismus).

Causes of hypertonia

- UMN lesion (spastic, may be clasp knife).
- Extrapyramidal lesion (leadpipe or cogwheel).
- Conversion disorder (rigidity continues to increase with more and more passive movement).
- Others: Catatonic state, tetanus and strychnine poisoning.

Causes of hypotonia

- LMN lesion (due to any cause).
- Cerebellar lesion (knee jerk may be pendular).
- Dorsal column lesion.
- Polyneuropathy.
- Hypokalaemia or hyperkalaemia.
- Drug: Any muscle relaxant.

Q: What is **upper limb drift?**

A: Normally, outstretched hands in front are held symmetrically even when the eyes are closed. In UMN lesion, when the upper limbs are outstretched with the palm uppermost, affected limb drifts downwards and medially, forearm tends to pronate and hands flex slightly at fingers.

Q: How **reinforcement** helps or acts?

A: Reinforcement acts by increasing the excitability of anterior horn cells and by increasing the sensitivity of muscle spindle primary sensory endings to stretch by increased gamma fusimotor drive.

Q: What are the **causes** of loss of tendon reflex?

A: As follows:

- LMN lesion.
- Peripheral neuropathy.
- Dorsal column lesion.
- Hypokalaemia or hyperkalaemia.

Isolated **loss of jerk** indicates radiculopathy of the affected segment (such as disc prolapse):

- Loss of biceps (C**5,6** lesion).
- Loss of triceps (C**6,7** lesion).
- Loss of ankle jerk (S**1** lesion).

Q: What are the causes of **extensor plantar response?**

A: As follows:

- First year of life (due to lack of myelination of pyramidal tract. Myelination occurs in 6–12 months).
- Sleep.
- UMN lesion.
- Deep coma (due to any cause).
- Postepileptic period (after grand mal seizure).

Spastic Paraplegia (Spinal Cord Compression)

Usual instructions are:

- Examine the lower limbs or perform the neurological examination of the lower limbs.

Proceed to examine the lower limbs as described before. If there is any sensory loss, find out the level. Always look at the back to find any scar, bony deformity, and gibbus or local tenderness in spine. Later, examine the upper limbs also.

Presentation of a Case

- The patient has slight wasting of right or left, or both thigh or leg (mention, if any).
- There is hypertonia in both lower limbs (may be clasp knife).
- Both flexor and extensor muscles of lower limbs are weak (mention the grade).
- Knee and ankle jerks are exaggerated on both sides.
- Plantar response is extensor on both sides.
- There is ankle clonus in right or left or both (mention, if any).
- Coordination is impaired in right or left or both (mention, if any).
- Loss of sensation in right or left or both (mention, up to where).
- Vibration and position senses are normal.
- There is no spinal deformity or tenderness or any surgical scar over the spine.
- Gait: Scissor gait.
- Rombergism is absent.

My diagnosis is **spastic paraplegia,** more likely due to spinal cord compression.

Q: What are the **causes** of spastic paraplegia?

A: As follows (remember the age and also sensory loss):

- Spinal cord compression due to any cause (see below).
- Demyelinating disease (in MS).
- Motor neuron disease (in middle-aged or elderly).
- Friedreich ataxia (in early age).
- Hereditary spastic paraplegia.
- SCD.

Q: What are the **cardinal signs** of spinal cord compression?

A: As follows:

- UMN signs (spastic paraplegia).
- Segmental sensory loss (sensory loss up to a particular segmental level).

Q: What are the other **features** of spinal cord compression?

A: As follows:

- Sphincter disturbance: Common (urinary retention and loss of bladder control).
- Root pain: Frequent at the site of compression.
- Pain radiates in a band around the chest (thoracic compression).

Q: Could it be due to **MND?**

A: Unlikely, because in MND there will be:

- No sensory loss (very important sign).
- Fasciculation.
- Age (usually above 40 years).

Q: Could it be due to **Friedreich ataxia?**

A: In Friedreich ataxia, there will be:

- Early age.
- Pes cavus and kyphosis.
- Loss of knee and ankle jerk, plantar is extensor.
- Signs of cerebellar lesion.

Signs of posterior column lesion (loss of vibration and position sense).

Q: What are the **other findings in Friedreich ataxia?**

A: Optic atrophy, high arched palate, deafness and cardiomyopathy.

Q: Could it be due to **subacute combined degeneration?**

A: Unlikely, as in SCD there will be:

- Peripheral neuropathy.
- Posterior column lesion.
- Knee and ankle jerk absent (knee jerk may be brisk; plantar may be extensor).
- Romberg sign is positive.
- Others: Anaemia and smooth shiny tongue with atrophy of papilla.

N.B. Remember to diagnose the cause of spastic paraplegia:

- If spastic paraplegia with sensory loss with a definite upper limit: It is likely to be due to **spinal cord compression.**
- If plantar response is extensor, sensory loss in glove and stocking pattern with loss of vibration and position sense: It is likely to be due to **SCD.**
- If cerebellar signs are present: The diagnosis is MS or Friedreich ataxia.
- In young patient with pes cavus, dorsal column lesion and cerebellar signs: The likely diagnosis is Friedreich ataxia.
- If spastic paraplegia, but no sensory loss: The likely diagnosis is MND (amyotrophic lateral sclerosis; also LMN lesion in upper limb).

Q: What are the **causes of paraplegia of sudden onset?**

A: As follows:

- Trauma (to vertebral column).
- Collapse of vertebra due to any cause.
- MS.
- Anterior spinal artery occlusion.
- Dissecting aneurysm.
- Haematomyelia.
- Postinfectious or postvaccinal myelitis (transverse myelitis).
- Paraplegia in flexion: Due to partial transection of spinal cord where the limbs are involuntarily flexed in hips and knees (because extensor muscles are more paralysed than flexors).
- Paraplegia in extension: Due to complete transection of spinal cord. (Flexors are more paralysed than extensors. There is coincidental involvement of spinal extrapyramidal tracts.)

Q: What are the **commonest causes** of spastic paraplegia?

A: As follows (7 Ts):

- Trauma.
- Tuberculosis (Pott disease).
- Tumour (meningioma, neurofibroma, lymphoma, leukaemia, myeloma, glioma).
- Transverse myelitis.
- Tabes dorsalis.
- Twelve (B_{12} deficiency).
- Thrombosis.

Q: What are the **causes** of spinal cord compression?

A: As follows:

1. Extradural (lesion in vertebral column):
 - Trauma.
 - Tuberculosis (TB) of spine (Pott disease).
 - Lymphoma.
 - Secondary deposit (elderly).
 - Multiple myeloma (elderly).
 - Abscess (paravertebral).
2. Intradural (extramedullary and intramedullary):
 a. Extramedullary causes (within dura):
 - Meningioma.
 - Neurofibroma.
 - Secondary deposit (elderly).
 - Lymphoma.
 - Leukaemia.

 b. Intramedullary causes:
 - Glioma.
 - Ependymoma.
 - Syringomyelia.
 - Haematomyelia.



Gibbus in tuberculous spondylitis



Cerebral palsy—spastic diplegia

Q: How to **find out** the sensory level in spinal cord compression?

A: In the following ways:

Vertebral level	Spinal cord segment
Cervical vertebrae	Add 1
Upper-thoracic vertebrae (T1–T6)	Add 2
Mid-thoracic vertebrae (T7–T9)	Add 3
Xth thoracic vertebra	Lumbar 1 and 2
XIth thoracic vertebra	Lumbar 3 and 4
XIIth thoracic vertebra	Lumbar 5
First lumbar vertebra	Sacral and coccygeal cord segments

Q: What are the **causes** of spastic paraplegia due to cerebral lesion?

A: As follows:

- Parasagittal meningioma (usually involving falx meningioma).
- Thrombosis of superior longitudinal sinus.
- Thrombosis of unimpaired anterior cerebral artery.
- Multiple cerebral infarctions.
- Hydrocephalus.
- Trauma.
- In children, cerebral palsy (usual lesion is bilateral parasagittal cortical lesion).

Q: What are the **features** of cerebral lesion causing paraplegia?

A: As follows:

- There is bladder disturbance (urinary retention).
- Cortical type of sensory loss.
- Other features: Headache, vomiting, convulsion, Jacksonian fit.

N.B. Lower limbs and micturition centre are represented in the paracentral lobule. Hence, lesion in this area produces paraplegia associated with bladder dysfunction.

Q: What are the **noncompressive causes** of spastic paraparesis or paraplegia?

A: As follows:

- MND (e.g. amyotrophic lateral sclerosis).
- Subacute combined degeneration.
- Transverse myelitis.
- MS.
- Friedreich ataxia.
- Lathyrism.
- Syringomyelia.
- Vascular disease of the cord.
- Hereditary spastic paraplegia.
- Tropical spastic paraplegia.
- Postvaccination.
- Syphilitic amyotrophy.
- Nonmetastatic manifestation of malignancy.
- Radiation myelopathy.
- Functional.

According to the type of lesion:

- Demyelinating: MS, acute demyelinating encephalomyelitis (ADEM).
- Inflammatory: Sarcoidosis, postviral, postvaccinal.
- Infective: HIV, Herpes zoster, Herpes simplex, syphilis.
- Degenerative: MND, familial spastic paraplegia (FSP), SCD, Friedreich ataxia (FA).
- Vascular: Anterior spinal artery infarction, intramedullary haemorrhage, spinal arteriovenous malformation (AVM).
- Toxic: Lathyrism, radiation.

Q: What are the **differences** between compressive and noncompressive paraplegia?

A: As follows:

Topic	Compressive	Noncompressive
Onset	Gradual	May be acute
Symmetry	Asymmetrical	Usually symmetrical
Root pain	Present	Absent

Bony deformity	Present	Absent
Bony tenderness	Present	Absent
Hyperaesthesia or girdle-like sensation	Present	Absent
Upper level of sensory loss	Present	Absent
Flexor spasm	Common	Uncommon
Bladder and bowel involvement	Usually early feature	Usually late feature; may be early in acute transverse myelitis.

Q: What **investigations** are done in spastic paraplegia?

A: As follows:

- X-ray of lumbodorsal spine [anteroposterior (AP) and lateral view].
- CT scan or MRI of spine.
- Lumbar puncture and cerebrospinal fluid (CSF) study.
- Other tests on the basis of cause (e.g. tuberculosis and multiple myeloma).

Q: What is **paraplegia in flexion** and **paraplegia in extension**?

A: As follows:

- Paraplegia in extension: It indicates an increase in the extensor muscle tone leading to an extension of the lower limbs (hip and knee extended; feet plantar flexed). It is due to involvement of pyramidal tracts from partial transection of spinal cord, but the extrapyramidal tracts (especially vestibulospinal tracts) are intact. May change to paraplegia in flexion if the damage to the spinal cord is more extensive and the vestibulospinal tracts are destroyed.
- Paraplegia in flexion: Lower limbs are flexed (in hips and knees; feet are dorsiflexed). It is due to complete transection of spinal cord. Both pyramidal and extrapyramidal tracts are affected.

Paraplegia in extension and paraplegia in flexion follows severe injury to the spinal cord.

Q: What are the **differences** between paraplegia in extension and flexion?

A: As follows:

Points	Paraplegia in extension	Paraplegia in flexion
Cause	Pyramidal lesion	Pyramidal and extrapyramidal
Hypertonia	More in extensor group of muscles	More in flexor group of muscles
Position of lower limbs	Extended	Flexed
Deep reflexes	Exaggerated	Less exaggerated
Clonus	Present	Absent
Mass reflex	Absent	May be present
Bladder	Precipitancy	Automatic bladder

Q: What is **mass reflex**?

A: Following stimulation of skin of the lower limbs or lower abdominal wall, there is reflex flexion of the lower trunk muscles and the lower limbs, evacuation of the bladder, bowel and semen, and sweating called mass reflex. This reflex indicates severe spinal cord lesion.

Q: What are the causes of **absent ankle jerk, but extensor plantar response?**

A: As follows:

- Subacute combined degeneration of the spinal cord.
- Friedreich ataxia.
- MS.
- Taboparesis.
- Diabetes mellitus with cervical myelopathy.

Q: What are the findings of spinal cord compression at different **levels** of spinal cord?

A: As follows:

- **Lesion above C5:** UMN lesion in both upper and lower limbs with loss of sensation in all four limbs.
- **Lesion at C5:** LMN lesion in proximal muscles of upper limbs (rhomboid, deltoid, biceps, brachioradialis) with segmental loss of sensation and UMN lesion in rest of the upper limbs and in lower limbs. Biceps reflex is lost and triceps jerk is exaggerated.
- **Lesion at C8:** LMN lesion and wasting of the intrinsic muscles of the hand and UMN lesion in lower limbs. There is segmental loss of sensation.
- **Lesion in thoracic cord:** Spastic paraplegia with segmental sensory loss. (Loss of upper abdominal reflexes at T7 and T8. Loss of lower abdominal reflexes and upward displacement of the umbilicus at T10 and T11).
- **Lesion at L1:** UMN lesion in lower limbs and cremasteric reflex is lost (normal abdominal reflex).
- **Lesion at L4:** LMN lesion and wasting of quadriceps; loss of knee jerk but hyperreflexia of ankle jerk and extensor plantar response.
- **Lesion in L5 and S1:** LMN weakness of knee flexion and hip extension (S1) and abduction (L5),

and calf and foot muscles. Knee jerk is present, but no ankle jerk or plantar response. Anal reflex is present.

- **Lesion in S3 and S4:** No anal reflex, saddle sensory loss, normal lower limbs.

Q: What is the **difference** between rigidity and spasticity?

A: As follows:

1. Spasticity means increased resistance during the initial part of passive movement, followed by lessening of the resistance.
 - It may be clasp-knife type, in which there is more resistance at the onset of movement followed by sudden loss of resistance. It is due to pyramidal lesions. Spasticity is better felt with attempting extension of upper limbs and flexion of lower limbs. It is associated with other signs of UMN lesion. It involves only the antigravity muscles (extensors of the upper limbs and flexors of the lower limbs).
2. Rigidity means sustained uniform resistance during passive movement. Rigidity is found in extrapyramidal lesion and involves all groups of muscles. It may be:
 - Lead pipe in which resistance is uniform throughout the passive movement (better seen in elbow and knee).
 - Cog wheel in which continuous resistance is interrupted by tremor (better seen in the wrist and ankle joints).

Q: How to **treat** spastic paraplegia?

A: As follows:

1. General measures:
 - Physiotherapy.
 - Nutritional support.
 - Care of bowel and bladder (if needed, catheterization).
 - Change of position to prevent bedsore. Special bed may be used.
 - For spasm: Baclofen, tizanidine, gabapentin, botulinum toxin, etc. Intrathecal baclofen or phenol may be tried.
2. Specific measures:
 - Neurosurgical intervention: For any tumour, selective dorsal rhizotomy. (Cutting selective nerve roots between L2 and S2; it is useful in cerebral palsy patient.)
 - Orthopaedic measures.
 - Treatment of primary cause.

Monoplegia (Brown–Séquard Syndrome)

Usual instructions are:

- Examine the lower limbs. Or perform the neurological examination of the lower limbs.

Presentation of a Case (Supposing Right Lower Limb)

- There is hypertonia and weakness of extensors and flexors of knee and ankle.
- Knee and ankle jerks are exaggerated; plantar is extensor.
- No sensory impairment, but loss of vibration and joint position sense.
- In the left lower limb: Loss of pain and temperature extending up to just below umbilicus (T8,9), but vibration and joint position sense and light touch are intact.

My diagnosis is **hemisection of spinal cord in the right side (Brown–Séquard syndrome).**

Q: What is **Brown–Séquard syndrome?** What are the **causes?**

A: It is due to the damage on one side or hemisection of the spinal cord characterized by:

1. On the side of lesion:
 - At the level: Band of hyperaesthesia and LMN lesion.
 - Below the level: Loss of vibration and position sense (posterior column), and UMN lesion (ipsilateral).
2. Contralateral (opposite) side: Loss of pain and temperature (spinothalamic tract lesion) below the level of lesion, giving rise to dissociated sensory loss.

Causes of Brown–Séquard syndrome:

- Compression of spinal cord tumour (glioma or angioma).
- MS.
- Myelitis.
- Trauma.
- Radiation myelopathy.

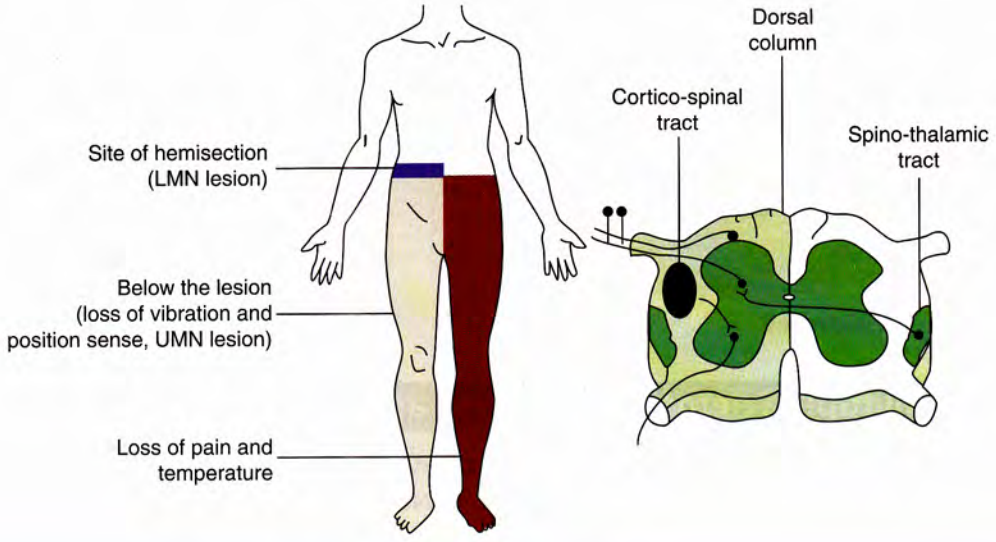
The patient complains of numbness of one side, whereas weakness, heaviness and stiffness on other sides.

N.B. If lesion is high up (C5,6), there may be hemiplegia as well.

Q: What **investigations** should be done?

A: As follows:

- MRI of the spinal cord.
- Others: According to suspicion of cause, e.g. CSF study, viral serology, vitamin B_{12} level, syphilitic serology (if any).



Monoplegia

Usual instructions are:

- Perform neurological examination of lower limbs.

Presentation of a Case (Supposing Right Side)

- Right lower limb is short and pes cavus is present.
- There is wasting of muscles with hypotonia.
- Muscle power is diminished, grade 3/5.
- Knee and ankle jerks: Diminished (or absent).
- Plantar: Normal (or equivocal).
- There is no sensory abnormality.
- Vibration and position senses are normal.
- Coordination: Impaired.

My diagnosis is **monoplegia of the right lower limb.**

Q: What are the **causes?**

A: As follows:

- Old poliomyelitis.
- Hemiatrophy.

Q: What is the **site of lesion** in poliomyelitis?

A: Anterior horn cell of the spinal cord (commonly in lumbar region).

Q: What is the **site** of lesion of weakness of one limb or monoplegia?

A: Brachial plexus (upper limb), lumbosacral plexus (lower limb) and central lesion (in motor cortex or partial internal capsule lesion).

Q: What is the **sensory** abnormality in poliomyelitis?

A: Usually, no sensory abnormality.

Q: What is the **cause** of poliomyelitis?

A: It is caused by polio virus, which is an enterovirus in the picornaviridae family. It is of three types:

- Type I: Brunhilde.
- Type II: Lansing.
- Type III: Leon.

Q: What are the types of vaccine for polio myelitis?

A: Two types:

- Oral live attenuated polio virus (OPV) or Sabin vaccine.
- Inactivated polio virus (IPV) or Salk vaccine.

Q: What are the types of polio?

A: They are of four types:

- Abortive: Characterized by fever, myalgia, sore throat, etc. Self-limiting.
- Nonparalytic: Above features plus signs of meningeal irritation. Complete recovery occurs.
- Paralytic: Above features that subside in 4–5 days recur with signs of meningeal irritation, muscular pain followed by asymmetric flaccid paralysis.
- Bulbar polio: Characterized by cranial nerve involvement and respiratory muscle paralysis. Also, soft palate, pharyngeal and laryngeal muscle paralysis is common.



Hemiatrophy



Old poliomyelitis

Multiple Sclerosis (Presenting as Spastic Paraplegia)

Usual instructions are:

- Perform neurological examination of lower limbs.
- Examine the eye or fundoscopy (optic atrophy and nystagmus: See Chapter 10, 'Examination of the Eye').
- Test for cerebellar signs (see in the 'Cerebellar Lesions' in this chapter).

Presentation of a Case

- Presents as described in spastic paraplegia; **plus** there may be slight sensory abnormality, but no definite upper limit.

My diagnosis is **spastic paraplegia,** more likely multiple sclerosis (MS).

Q: What are the **differential diagnoses**?

A: As follows:

- Spinal cord compression.
- Subacute combined degeneration.
- Neurosyphilis.
- Neurosarcoid.

Q: What are the **causes** of bilateral upper motor neuron lesion involving the lower limbs?

A: As follows:

- Spinal cord compression.
- MS.
- MND (amyotrophic lateral sclerosis).
- Hereditary spastic paraplegia.
- Transverse myeliltis.
- Subacute combined degeneration.
- Friedrich ataxia.
- Bilateral cerebral infarction.
- Cervical myelopathy.

Q: Why not **spinal cord compression?**

A: No definite upper limit of sensory loss.

Q: If it is MS, what **relevants** do you want to see?

A: As follows:

- Eye: Nystagmus, and optic neuritis or optic atrophy.
- Signs of cerebellar lesions (see in 'Cerebellar Lesion' in this chapter).
- Abdominal reflex (early loss).
- Urinary incontinence, impotence and constipation **(triad of Steinberg).**

Q: What are the **presentations** of MS?

A: Twice more common in females. Age of onset is 20–45 years. Before puberty and after 60 years, it is rare. The patient usually presents with:

- Weakness of one or more limbs.
- Optic neuritis (patient complains of blurring of vision).
- Features of spastic paraplegia (confused with spinal cord compression).
- Features of cerebellar signs (ataxia and tremor, etc).
- Features of brainstem dysfunction (vertigo, diplopia, nystagmus, facial numbness or weakness, dysarthria, dysphagia and pyramidal signs in limbs).
- Bladder dysfunction (incontinence, dribbling and hesitancy).
- Sensory disturbance: Tingling of the extremities and light banding sensation around the trunk or limbs (due to posterior column involvement).
- Others (rarely): Epilepsy, trigeminal neuralgia, facial palsy (may be recurrent), VIth nerve palsy, tonic spasm or brief spasm of limbs, dementia, neuropsychiatric dysfunction, depression.
- Euphoria despite disability.

Common mode of onset:

1. Optic neuritis (25%).
2. Transverse myelitis (like spinal cord compression).
3. Cerebellar ataxia.
4. Various brainstem syndromes: Vertigo, facial pain or numbness, dysarthria, diplopia.

Signs and symptoms of MS (remember the mnemonic: WATSON)

- **W:** Weakness.
- **A:** Ataxia (cerebellar).
- **T:** Tremor (cerebellar).
- **S:** Speech (scanning).
- **O:** Optic neuritis.
- **N:** Nystagmus.

Q: What **investigations** should be done in MS?

A: As follows:

1. MRI of brain and spinal cord: Investigation of choice. It shows multiple plaques, hyperintense in T2W and FLAIR mainly in the periventricular region, corpus callosum, cerebellar peduncles, juxtacortical posterior fossa, brainstem and subpial region of spinal cord. CT scan is not sensitive.
2. Lumbar puncture and CSF study. [There is slight increase in lymphocyte, increase in total protein in (40%) cases, and oligoclonal band in (70–90%) cases, mainly IgG on electrophoresis.]
3. Evoked potential: Mainly VEP (visual evoked potential) is usually delayed, if there is optic nerve involvement.
4. To exclude other conditions:
 - Chest X-ray (to exclude bronchial carcinoma).
 - X-ray of spine (to exclude cord compression).
 - Serum angiotensin converting enzyme (to exclude sarcoidosis).
 - Serum B_{12} (to exclude subacute combined degeneration of spinal cord).
 - ANA (to exclude SLE).
 - Antiphospholipid antibodies.

Q: What is the **role of MRI**?

A: MRI is the single most investigation to confirm the diagnosis of MS, positive in 80% cases. It shows hyperintense focal periventricular white matter lesions in T2-weighted (T2W) images. Although, these are typical, but not pathognomonic and may be found in small infarcts, disseminated metastases, Moyamoya disease and inflammatory diseases.

MRI in MS is helpful for the following:

1. Reveals asymptomatic plaques in cerebrum, brainstem, optic nerves and spinal cord.
2. MS plaques are hyperintence on T2W and even more strikingly obvious on fluid attenuated inversion recovery (FLAIR).
3. On T2W, several asymmetrical, well-demarcated lesions immediately adjacent to ventricular surface (periventricular lesion) usually denote MS. Especially diagnostic are oval or linear regions of demyelination oriented perpendicularly to the ventricular surface. When viewed on sagittal images, they extend outward from corpus callosum in fimbriated pattern termed 'Dawson fingers'.
4. Another characteristic pattern is C-shaped partial ring of enhancement created by rounded lesion interrupted by gyrus.
5. Lesions that have undergone some degree of cavitation are hypointense on T1-weighed (T1W) images termed 'black holes'.
6. Serial MRI can demonstrate progress of disease, e.g. increasing number of lesions.
7. MRI changes assume maximum diagnostic significance when they are consistent with the clinical findings.

Q: What are the **clinical courses (or types)** of MS?

A: As follows:

- Relapsing and remitting MS (80–90%): The patient suffers from episodes of acute worsening with recovery and remains stable between relapses.
- Primary progressive MS (10–20%): Gradual neurological deterioration from the onset. It usually begins after 40 years (late onset).
- Secondary progressive MS: Some cases of relapsing and remitting course show gradual neurological deterioration. There may be superimposed acute relapses.
- Fulminating MS (<10%).

Q: What is **MS? What is the natural history** of the disease?

A: It is a demyelinating disorder of central nervous system (CNS) characterized by multiple plaques of demyelination within the brain and spinal cord, gliosis and varying degrees of inflammation. Usually there is relative preservation of axons.

Natural history is extremely variable—may be acute, subacute, insidious, relapsing and remitting, chronic progressive, spontaneous recovery, and rapidly progressive and secondarily progressive.

It is also called disseminated sclerosis, as the plaques are **disseminated both in time and space.** Presence of two neurological lesions in anatomically unrelated sites or at different times indicates MS.

Q: What are **sites of involvement** in MS?

A: As follows:

- Optic nerve.
- Brainstem.
- Cerebellum.
- Periventricular region.
- Spinal cord (posterior column and corticospinal tract).

Q: What are the **prognostic factors** in MS?

A: As follows:

1. Good prognostic factors:
 - Early age of onset.
 - Relapsing and remitting form of disease.
 - Visual or sensory symptoms alone at presentation.
 - Minimum neurological impairment 5 years after onset.
 - More benign course in women than in men.
 - Little residual disability 5 years after onset.
2. Poor prognostic factors:
 - Old age >40 years.
 - Frequent relapse in first 2 years.
 - Short interval between first two relapses.
 - Pyramidal, brainstem and cerebellar symptoms.
 - Primary progressive disease.
 - Poor recovery from relapse.
 - MRI shows many lesions.

Q: What are the **other demyelinating disorders?**

A: As follows:

- Devic disease (acute necrotising myelitis with optic neuritis).
- Tuberous sclerosis (patchy demyelination).
- Leukodystrophies.
- Schilder disease (diffuse cerebral sclerosis). There may be cortical blindness if occipital cortex is involved. Other features are cerebral deafness, quadriplegia, hemiplegia, dementia, pseudobulbar palsy.
- Acute disseminated encephalomyelitis (ADEM).

Q: What are the **features** of end-stage MS?

A: In end-stage disease, the patient is severely disabled with spastic paraplegia, tetraplegia, ataxia, optic atrophy with blindness, pseudobulbar palsy, urinary incontinence, brainstem dysfunction and dementia.

Q: What is **Uhthoff** phenomenon?

A: Exaggeration of symptoms after hot bath is called Uhthoff phenomenon. The patient feels extreme weakness after hot bath. It is due to heat-induced conduction block of partially demyelinated fibres.

Q: What is **Lhermitte sign?**

A: When the neck is flexed, there is tingling or electric shock-like sensation or funny sensation that passes down in the upper limb, trunk and perhaps lower limbs called Lhermitte sign (also called barber's chair sign). It indicates that the disease is near the dorsal column nuclei of higher cervical cord (indicates cervical cord compression). Causes are:

- MS (the commonest cause, especially in acute exacerbation).
- Cervical spondylosis.
- Cervical cord compression (by tumour).
- Subacute combined degeneration.
- Radiation myelopathy.
- Cervical spondylotic myelopathy.

N.B. A similar sensation provoked by neck extension may occur called **reverse Lhermitte sign.** It strongly suggests cervical spondylosis.

Q: What happens during **pregnancy** in MS?

A: Mild protective effect during pregnancy. Exaggeration may occur in puerperium.

Q: What are the **causes** of MS?

A: Unknown, the following factors may be associated:

- Environmental factors: More in temperate zone, and rare in tropical country. Greater among rural than urban dwellers.
- More frequent in the higher socioeconomic group.
- Genetic: Ten times more in first-degree relative.
- Immunological: There is an increase in activated T-lymphocyte in CSF, increase in immunoglobulin in CNS and increase in antibody to some virus (measles).
- Diet: More in those who eat animal fat.
- HLA association – DR2, DR3, B7, A3.

Q: How to **treat** MS?

A: As follows:

1. During acute attack:
 - Intravenous methylprednisolone: 1 g for 3 days or oral 500 mg for 5 days. It shortens the duration of relapse but does not affect the long-term outcome, followed by oral prednisolone 40 mg daily for 10 days, then 20 mg for 2 days and then 10 mg for 2 days.
 - Or, high-dose prednisolone: 40–60 mg daily for 10 days, then tapered over for 2 days (It has no role for long-term use for prevention.)
 - Plasmapheresis is sometimes helpful in patient with severe relapse and unresponsive to corticosteroid.

2. To prevent relapse (disease-modifying drugs may be given):
 - Immunosuppressive drug: Azathioprine may be helpful. (cyclophosphamide, sometimes helpful in aggressive disease, is not recommended for widespread use.) Mitoxantrone may be helpful.
 - Subcutaneous or intramuscular β interferon (1a or 1b) reduces number of relapse (30%).
 - Glatiramer acetate has similar effect. It has immunomodulatory effect.
 - Monoclonal antibody to β-integrins (natalizumab) or to lymphocyte epitopes (campath-1H) or alemtuzumab may be helpful in severely affected patient.
 - IV immunoglobulin may be helpful in aggressive cases.
3. Supportive and symptomatic treatment for complication and disability:
 - For incontinence: Intermittent self-catheterization drugs like oxybutynin, tolterodine, etc.
 - Urgency or frequency: Intermittent self-catheterization is advised if postmicturition residual urine is >100 mL. If it is <100 mL, oxybutynin or tolterodine may be given.
 - For spasticity: Physiotherapy and drugs like baclofen (oral or intrathecal), tizanidine, benzodiazepine or dantrolene may be used. Local intramuscular injection of botulinum toxin or chemical neuronectomy is other option. Cannabis extracts and synthetic cannabinoids are also used.
 - For dysaesthesia: Carbamazepine, gabapentin, phenytoin or amitriptyline may be helpful.
 - For ataxia: Isoniazid (INH) or clonazepam.
 - For fatigue: Amantadine, modafinil or amitriptyline.
 - For impotence: Sildenafil may be used.
 - Control of infection.
 - Prevention of pressure sore.
 - Rehabilitation, occupational therapy, walking aids, visual aids, etc.
 - Counselling, patient's education.

Q: What is the **role of steroid** in MS?

A: In MS with optic neuritis, high-dose intravenous methylprednisolone for 3 days followed by short course of prednisone may be given. It reduces the rate of relapse of MS over 2 years.

Q: What is the **role of exercise** in MS?

A: The patient should be active during remission and avoid excessive physical exercise during relapses.

Q: What is the **indication** of interferon β-therapy?

A: It is used only in patient with relapsing remitting type of MS who had at least two relapses in the previous 2 years and who are able to walk unaided.

N.B. Remember the following points in MS:
- Common in women of 20–40 years of age (rare before puberty and after 60 years, F:M = 2:1).
- It is called disseminated sclerosis, as it is **disseminated in time and place.**
- Patient may complain of blurring or loss of vision. Using fundoscopy nothing is seen. ('If doctor sees nothing, patient sees nothing'. This is due to retrobulbar neuritis.)
- Peripheral nervous system is spared; only CNS involvement.
- Causes of death are uraemia and bronchopneumonia.

Flaccid Paraplegia (GBS)

[Common cases in flaccid paraplegia are Guillain–Barré syndrome (GBS) and peripheral neuropathy.]

Usual instructions are:
- Examine the lower limbs. Or, perform the neurological examination of the lower limbs.

Presentation of a Case

- There is wasting of muscles in both lower limbs (mention, up to where) with hypotonia.
- Muscle power is diminished, grade 2/5 (mention where).
- Both knee and ankle jerks: Diminished or absent (ensure that you have done reinforcement).
- Plantar: Normal or equivocal on both sides.
- There is no sensory abnormality (may be some sensory abnormality; mention if any).
- Vibration and position senses are normal.
- Coordination: Could not be elicited due to weakness.
- Gait: Unable to walk due to weakness.

My diagnosis is **flaccid paraplegia,** which is more likely due to GBS.

Q: What are the **causes** of flaccid paraplegia?

A: As follows:

- GBS.
- Motor neuropathy due to any cause.
- Tabes dorsalis.
- Friedreich ataxia.
- Progressive muscular atrophy (one type of MND).
- Acute inflammatory demyelinating polyradiculopathy (AIDP).
- Hysterical conversion reaction (HCR).

Q: What are the causes of **predominant motor neuropathy?**

A: As follows:

- GBS.
- Charcot–Marie–Tooth disease.
- Acute intermittent porphyria.
- Chronic lead poisoning.
- Diabetic amyotrophy.
- Diphtheria.
- Paraneoplastic syndrome.

Q: If it is GBS, what **else** do you want to examine?

A: As follows:

- In the upper limb: Both may show features of flaccid weakness (all four limbs may be paralysed at the same time).
- Loss of all reflexes (an important clue).
- Cranial nerve: Bilateral facial palsy may occur.
- Fundoscopy: Papilloedema may be present.

Q: How does the patient of GBS usually **present?**

A: As follows:

- History of upper respiratory tract infection (URTI) or gastroenteritis (viral or bacterial).
- After 1–3 weeks, there is weakness of lower limbs that ascends over several weeks (ascending paralysis). It may advance quickly thereby affecting all the limbs at once and can lead to paralysis (quadriplegia).
- Respiratory paralysis in 20% case. Progressive respiratory involvement and paralysis is the main problem.
- Paraesthesia and pain in back and limbs may occur.
- Facial and bulbar weakness.
- Autonomic dysfunction: Change of blood pressure, tachycardia, increased sweating; dysrhythmia may occur.

Brief clinical findings in GBS:

- Flaccid paralysis involving lower limbs and may involve all four limbs.
- Loss of all reflexes.
- Bilateral facial palsy in 50% cases, unilateral facial palsy in 25% cases.
- Sensory loss: Minimum or absent.
- Sphincter involvement (rare).

N.B. Remember the following points:

- Diffuse weakness with loss of all reflexes: A very striking finding in GBS.
- GBS may be associated with Hodgkin lymphoma.
- Papilloedema may develop.
- May develop **syndrome of inappropriate antidiuretic hormone** (SIADH).

Q: What are the **dangerous complications** of GBS **(cause of death)?**

A: As follows:

- Respiratory muscle paralysis. The patient may develop respiratory failure within hours.
- Bulbar palsy (dysphagia, nasal regurgitation).
- Cardiac conduction block.
- Cardiac arrhythmia.

Q: What is **GBS?**

A: It is a post-infective demyelinating neuropathy of unknown cause, usually 1–3 weeks after respiratory infection, diarrhoea, and occasionally after vaccination or surgery. There is demyelination of peripheral nerve or spinal root, which is immunologically mediated. This may follow after infection with cytomegalovirus or *Mycoplasma* or *Campylobacter jejuni*. GBS is monophasic and does not recur.

Q: What is the **cause** of GBS? What is the **mechanism?**

A: GBS develops 1–3 weeks after respiratory infection or diarrhoea (mainly by *Campylobacter*) in 70% cases. Triggering factors may be *Campylobacter jejuni*, cytomegalovirus (CMV), *Mycoplasma*, herpes zoster, human immounodeficiency virus (HIV), Epstein–Barr virus (EBV) infection.

There are two mechanisms:

1. Demyelinating [acute inflammatory demyelinating neuropathy (AIDP)].
2. Axonal, which may be:
 - Motor [acute motor axonal neuropathy (AMAN)].
 - Sensorimotor [acute motor and sensory axonal neuropathy (AMSAN)].

Q: What **investigations** do you suggest in GBS?

A: As follows:

- CSF analysis: Typical finding is 'albuminocytological dissociation' (albumin may be very high, >1000 mg%, lymphocytes are slightly raised or normal, <20/mm^3. If lymphocyte is >50, GBS is unlikely. CSF protein may be normal in first 10 days).
- Frequent monitoring of respiratory function tests [forced vital capacity (FVC), forced expiratory volume in 1 s (FEV_1), peak expiratory flow rate (PEFR)].
- Arterial blood gas analysis (as respiratory failure may occur at any time).
- Nerve conduction study. (It shows slow conduction or conduction block. Demyelinating neuropathy, usually found after 1 week.)
- Investigation to identify CMV, *Mycoplasma* or *Campylobacter* should be done.
- Serum electrolyte.

Note: Triad of acute symmetrical ascending paralysis of limbs, areflexia and albuminocytological dissociation in CSF is highly suggestive of GBS.

Q: What is **Miller–Fisher syndrome?**

A: It is a variant of GBS characterized by triad of ophthalmoplegia, ataxia and areflexia. It is a rare disease.

Q: How to **treat** GBS?

A: As follows:

- Ideally the patient should be treated in ICU and respiratory function should be monitored regularly (vital capacity and arterial blood gases). The patient may require artificial ventilation.
- High-dose intravenous γ-globulin should be given to all patients (it reduces the duration and severity). Dose is 400 mg/kg/day for 5 days. It is helpful, if given within 14 days. It may precipitate angina or myocardial infarction. In congenital IgA deficiency, it may cause allergic reaction.
- Plasma exchange if given within 14 days is equally effective in reducing the severity and duration of GBS.
- Steroid has no proven value (may worsen). Methylprednisolone with immunoglobulin has no proven benefit.
- Plasmapheresis may be required.
- Physiotherapy is the mainstay of therapy.
- Prevention of pressure sore and venous thrombosis.
- Other symptomatic treatment.

Indication of ventilation:

- Impending respiratory failure: Tachypnoea, decrease in arterial O_2 tension <85 mmHg, forced vital capacity (FVC) <20 mL/kg, maximum inspiratory pressure <30 cm H_2O, maximum expiratory pressure <40 cm H_2O.
- FVC <1.5 L.
- PaO_2 <10 kPa.
- $PaCO_2$ >6 kPa.
- Rapid progression of disease.
- Bulbar dysfunction.
- Bilateral facial palsy.
- Autonomic involvement.

Q: What is the **prognosis** of GBS?

A: As follows:

- 80% recovery, may take several months (3–6 months). If axons have been damaged, the regeneration may require 6–18 months or longer.
- 10% residual disability.
- 3–5% die (in some study up to 10% deaths).

Q: What are the bad and good **prognostic factors?**

A: As follows:

Adverse prognostic factors:

- Preceding GI infection.
- >60 years of age.
- The most severe or rapidly evolving form of the disease (maximum disability within 7 days).
- Descending paralysis.
- Bulbar weakness.
- Autonomic dysfunction.
- Asymmetrical weakness.
- Very high CSF protein.
- Evidence of widespread axonal damage.
- Those requiring early and prolonged mechanical ventilatory assistance.

Good prognostic factors:

- Symmetrical involvement.
- Slowly progressive.
- Facial nerve involvement.
- Young age.
- Preceding H/O respiratory infection.
- Demyelinating disease.
- No respiratory involvement.
- Ascending paralysis.
- Early treatment.
- Early recovery.

Polyneuropathy

Usual instructions are:

- Perform neurological examination of lower limbs or upper limbs.

Presentation of Case No. 1

- Present the case described in flaccid paraplegia page 325, plus:
- There is bilateral symmetrical sensory loss in stocking pattern with light touch and pin prick (mention up to where), and also loss of vibration and position senses.
- Gait is ataxic with wide based and high steppage.
- Rombergism is positive.

My diagnosis is **peripheral neuropathy (mixed motor and sensory type).**

Q: What do you think is the cause in this case?

A: As follows:

- Diabetes mellitus.
- Nutritional deficiency (B_1, B_6, B_{12}, folic acid, pantothenic acid and vitamin E).
- Malignancy, e.g. bronchial carcinoma (in elderly patients).
- Drugs (isoniazid, vincristine, phenytoin, amiodarone, statins, cisplatin and dapsone).
- Alcoholism.
- Infections (leprosy).
- Idiopathic.

Q: Could it be MND?

A: No. In MND, there is no sensory loss (fasciculation is present).

Presentation of Case No. 2

- Muscle power and tone are normal; reflexes are absent.
- There is bilateral symmetrical sensory loss in stocking pattern with light touch and pin prick (mention up to where); and also loss of vibration and position senses.
- Gait is ataxic with wide based and high steppage.
- Rombergism is positive.

My diagnosis is **peripheral neuropathy (predominant sensory type).**

Q: What are the causes of **predominantly sensory neuropathy?**

A: As follows:

- Diabetes mellitus.
- Leprosy.
- Deficiency of vitamins B_1, B_6 and B_{12}.
- Chronic renal failure.
- Paraneoplastic neuropathy (in bronchial carcinoma).
- Drugs (INH, vincristine).
- Hereditary sensory neuropathy.
- HIV.
- Multiple myeloma.

Presentation of Case No. 3

- There is wasting of all the muscles of lower limbs.
- Muscle power is diminished, grades 3/5 and 4/5.
- Knee and ankle jerks are diminished (or absent).
- Plantar response: Equivocal.
- Sensory is normal.

My diagnosis is **peripheral neuropathy (predominantly motor type).**

Q: What are the causes of **predominantly motor neuropathy?**

A: As follows:

- Guillain–Barré syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP)
- Charcot–Marie–Tooth disease.
- Acute intermittent porphyria.
- Chronic lead poisoning.
- Diabetic amyotrophy.
- Diphtheria.
- Paraneoplastic syndrome.
- POEMS (Peripheral neuropathy, Organomegaly, Endocrinopathy, M-protein, Skin changes).

Presentation of Case No. 4: Upper Limb

- There is wasting of the small muscles of hands, extending up to the middle part of both forearms.
- All the muscles are weak.
- There is bilateral symmetrical sensory loss in gloves pattern with light touch and pin prick (mention up to where).

My diagnosis is **peripheral neuropathy (mixed type).**

Q: What **else** do you want to examine in this case?
A: I want to examine the lower limbs to see any evidence of neuropathy.

Read the following topics in relation to polyneuropathy.

Q: What are the **causes** of peripheral neuropathy?
A: (Mention the causes according to the age of the patient):
- Diabetes mellitus.
- Nutritional deficiency (B_1, B_6, B_{12}, folic acid, pantothenic acid and vitamin E).
- Malignancy (bronchial carcinoma, lymphoma and multiple myeloma).
- Drugs [isoniazid (INH), vincristine, phenytoin, amiodarone, statins, cisplatin and dapsone].
- Alcoholism.
- Guillain–Barré syndrome.
- Infections (leprosy, HIV, typhoid and diphtheria).
- Collagen disease [systemic lupus erythematosus (SLE), polyarteritis nodosa (PAN) and rheumatoid arthritis (RA)].
- Others: Chronic renal failure (CRF), chronic inflammatory demyelinating polyneuropathy (CIDP) and idiopathic (in many cases).

Q: What are the **investigations** done in polyneuropathy?
A: As follows:
- Full blood count (FBC) and peripheral blood film (PBF) examination [evidence of megaloblastic anaemia in subacute combined degeneration (SCD)—macrocytosis].
- Blood sugar.
- Chest X-ray (bronchial carcinoma).
- Serum B_{12} and folate assay.
- Renal and hepatic function.
- Bone marrow (megaloblast in SCD).
- Other investigations according to suspicion of causes [antinuclear antibodies (ANAs) and RA test].
- Nerve conduction study [(NCS) (axonal or demyelinating)].

Q: What are the causes of **painful neuropathy?**
A: As follows:
- Diabetes mellitus.
- Deficiency of vitamins B_1 and B_{12}.
- Alcohol.
- Carcinomatous neuropathy.
- Porphyria.
- Arsenic or thallium poisoning.

Treatment: Tricyclic antidepressant, phenytoin, carbamazepine and topical capsaicin.

Q: What are the **mechanisms** of neuropathy?
A: As follows:
- Demyelination.
- Axonal degeneration.
- Wallerian degeneration (after section of nerve, axonal and myelin sheath degeneration).
- Compression (called entrapment neuropathy); and there is segmental degeneration at the site of compression.
- Infarction of nerve: microinfarction of nerve due to arteritis of vessels supplying nerve (diabetes mellitus and polyarteritis nodosa).
- Infiltration in nerve (leprosy, sarcoidosis and malignancy).

Q: What are the causes of **demyelination** and **axonal degeneration?**
A: As follows:
1. Causes of demyelination:
 - Guillain–Barré syndrome.
 - CIDP.
 - Hereditary sensory motor neuropathy.
 - Diphtheria.
 - Diabetes mellitus.
 - Refsum disease.
 - HIV.
2. Causes of axonal degeneration:
 - Toxic neuropathy (alcohol and drugs).
 - Diabetes mellitus.
 - Paraneoplastic.
 - IgG paraproteinaemia.
 - Hereditary.
 - Vitamin deficiency.

Q: How to **differentiate** between demyelination and axonal degeneration?
A: By NCS and electromyography (EMG):
- In demyelination, there is slowing of nerve conduction, amplitude of nerve action potential (CMAP) is normal.
- In axonal degeneration, the conduction velocity is normal as axonal continuity is maintained in surviving fibres, amplitude of CMAP is reduced. Using needle EMG, denervation on the affected muscles may be demonstrated.

Q: Which part is **first involved** in peripheral neuropathy? Why?
A: Usually distal part of the limbs is commonly involved, because longer the nerve fibre earlier is the involvement. Since the nerve fibres supplying the distal parts of the limbs are longer, they are first affected.

Q: What is **mononeuritis multiplex** and what are the causes of it?

A: Separate involvement of more than one peripheral nerve or cranial nerve by a single disease is called mononeuritis multiplex. It is due to involvement of vasa nervorum or malignant infiltration of nerves.

Causes are:

- Diabetes mellitus.
- Leprosy.
- Rheumatoid arthritis.
- Vasculitis (SLE, polyarteritis nodosa).
- Amyloidosis.
- Malignancy (carcinomatous neuropathy).
- Sarcoidosis.
- HIV infection.
- Wegener granulomatosis.
- Acromegaly.
- Paraproteinaemia.
- Lyme disease.
- Idiopathic multifocal motor neuropathy.

Causes of **acute mononeuritis multiplex** (usually vascular):

- Polyarteritis nodosa.
- Diabetes mellitus.
- Collagen disease (SLE and RA).

Q: What are the **types of neuropathy in DM?**

A: As follows:

- Commonly sensory neuropathy.
- Mixed motor and sensory neuropathy.
- Asymmetrical motor neuropathy (diabetic amyotrophy).
- Autonomic neuropathy.
- Mononeuropathy.
- Mononeuritis multiplex.

Mechanism of neuropathy in DM:

- Axonal degeneration.
- Patchy or segmental demyelination.

Involvement of intraneural capillaries.

Q: What are the **causes of thickening of nerves?**

A: As follows:

- Leprosy.
- Neurofibroma.
- Amyloidosis.
- Acromegaly.
- Sarcoidosis.
- Charcot–Marie–Tooth disease (hereditary motor and sensory neuropathy).
- Repeated friction or trauma.
- Refsum disease.
- Dejerine–Sottas disease (hypertrophic peripheral neuropathy).

Polyneuropathy [Subacute Combined Degeneration—(SCD)]

Usual instructions are:

- Perform neurological examination of lower limbs.

Presentation of a Case: Lower Limb

Present the case as described in "peripheral neuropathy" (page 328). However, knee jerk is brisk (ankle jerk is lost or absent) and planter is extensor.

My diagnosis is **peripheral neuropathy.**

Q: What do you think is the **cause** in this case and why?

A: I think this is a case of **SCD** because there are:

- Peripheral neuropathy.
- Signs of posterior column lesion (loss of vibration and position sense).
- Signs of pyramidal lesion (plantar is extensor, knee jerk is brisk and ankle jerk is absent).
- Rombergism is positive.

Q: What **else** do you want to see, if it is SCD?

A: As follows:

- Anaemia (may be lemon yellow pallor in pernicious anaemia).
- Glossitis (smooth tongue).
- Examination of abdomen may show: Mass of carcinoma stomach, or scar mark in the abdomen (if gastrectomy).
- Eye shows optic atrophy.
- Evidence of dementia.

N.B. Anaemia is usually present, but sometimes vitamin B_{12} neuropathy may not be associated with anaemia and there may be normal blood picture with normal marrow. Serum B_{12} should be measured.

Q: What **history** do you like to take in SCD?

A: As follows:

- Family history of pernicious anaemia.
- History of gastrectomy, resection of ileum.
- Frequent diarrhoea (Crohn disease).

- Patient's dietary habit (if the patient is vegetarian).
- History of chronic pancreatitis.
- History of infection with *Diphyllobothrium latum*.

Q: Why it is called **combined degeneration**? (Or, what is the lesion in SCD?)

A: Because there are:
- Posterior column lesion (degeneration of the ascending tract of the posterior column).
- Pyramidal lesion (degeneration of the descending pyramidal tracts in the lateral column).
- Demyelination of peripheral nerve (peripheral neuropathy).

Q: What are the **presentations** of SCD?

A: The patient usually complains of tingling or numbness, or burning sensation and weakness in the legs.

Q: Why **polyneuropathy** in SCD?

A: It is due to demyelination.

Q: What is the **type of anaemia** in SCD?

A: Macrocytic (megaloblastic) anaemia due to vitamin B_{12} deficiency.

Q: What **happens** if blood transfusion is given in vitamin B_{12} neuropathy with severe anaemia?

A: Blood transfusion or packed cell should be avoided without correcting vitamin B_{12}; otherwise neurological manifestation may be aggravated.

Q: What is the **daily requirement** of vitamin B_{12}? **How long** does it take to develop deficiency of vitamin B_{12}?

A: 1–2 mg daily. To develop deficiency, it takes 3 years.

Q: What are the **causes of** vitamin B_{12} deficiency?

A: As follows:
- Addisonian pernicious anaemia.
- Total gastrectomy (B_{12} injection should be given every 3 months) or partial gastrectomy (10–20% develop B_{12} deficiency within 5 years; B_{12} injection should be given every year).
- Ileal disease (Crohn disease, ileal resection).
- Stagnant loop syndrome.
- Pancreatic insufficiency (failure to transfer vitamin B_{12} from R-protein to intrinsic factor). Vegetarian diet.
- Chronic tropical sprue.
- Fish tapeworm (*D. latum*).
- Congenital intrinsic factor deficiency.

Q: What are the **clinical features** of SCD?

A: As follows:
- Age: 40–60 years, equal sex involvement.
- Sensory symptoms: Paraesthesia, tingling or numbness, starting in toes and fingers. Lower limbs are more commonly affected than the upper limbs.
- Motor symptoms: Weakness, ataxia and loss of all reflexes. May be exaggerated knee reflex with loss of ankle jerk, but extensor plantar.
- Bladder involvement: Urinary incontinence and dribbling (usually in late stage).
- Eye: Optic atrophy.
- Mental change: Dementia, impaired memory, confusion and depression.

Q: What **investigations** are done in SCD?

A: As follows:
1. FBC and PBF examination (macrocytosis and hypersegmented neutrophil).
2. Bone marrow (to see megaloblast).
3. Serum B_{12} assay.
4. Other investigations according to the suspicion of cause:
 - For Addisonian pernicious anaemia: Antiparietal cell and anti-intrinsic factor antibody, endoscopy and biopsy to see gastric atrophy, Schilling test.
 - Investigation for Crohn disease.

N.B. Macrocytosis in blood and megaloblastic marrow are invariable in SCD.

Q: How to **treat SCD**?

A: As follows:
- Injection of vitamin B_{12}: 1000 µgm intramuscular (IM), 5 doses, 2–3-days apart, then every 3 months for lifelong.
- Following therapy, iron deficiency may occur in the first few weeks. So, oral iron therapy should be given.
- Also, following therapy there may be hypokalaemia, which may need correction.
- B_{12} orally 2 mg/day may be given. 1–2% is absorbed by diffusion without intrinsic factor. Sublingual B_{12} may be effective.
- Treatment of primary cause.

Q: Will you **transfuse** blood in this patient?

A: Blood transfusion is avoided as it may precipitate heart failure. Also, before replacing B_{12}, if blood transfusion or packed cell is given, it may aggravate neurological manifestations. However, blood (or packed cell) transfusion may be considered if there is:
- Angina.
- Heart failure.
- Cerebral hypoxia (confusion, dizziness, etc.).

Q: How to see the **response**?

A: Clinical improvement may occur within 48 h; reticulocytosis may be seen after 2–3 days of starting therapy. Haemoglobin level rises by 1 g/dL every week.

Q: What is the **response** of neurological lesion to vitamin B_{12} therapy?

A: Response is variable. It may improve, remain unchanged or may even deteriorate. Sensory abnormalities improve more than the motor and peripheral neuropathy responses, better than myelopathy. Sensory neuropathy takes 6–12 months for recovery; longstanding polyneuropathy may not be improved.

Q: What are the **causes** of posterior or dorsal column lesion?

A: As follows:

- Subacute combined degeneration.
- Tabes dorsalis.
- Friedreich ataxia.
- MS.
- Brown–Séquard syndrome (ipsilateral leg).

N.B. Neurological features of vitamin B_{12} deficiency should be excluded in any patient with any of the following unexplained diseases:

- Peripheral sensory neuropathy.
- Spinal cord disease (posterior column lesion and corticospinal tract lesion).
- Optic atrophy (rare).
- Dementia (rare).
- Autonomic neuropathy.

Q: What are the **features of tabes dorsalis?**

A: As follows:

- Signs of dorsal column lesion (loss of vibration and position sense). Squeezing of the calf muscles and the Achilles tendon produces no pain (deep sensation is lost).
- Bladder involvement: Common.
- Eye signs: Argyll Robertson pupil and bilateral ptosis.
- Rombergism: Positive.

Motor Neuron Disease (MND)

Usual instructions are:

- Neurological examination of lower limbs or upper limbs.
- Look at the legs. What is your finding? (Fasciculation.) What else do you want to examine?
- Examine the hands (wasting).

Presentation of Case No. 1: Lower Limb

- There is wasting of all the muscles of lower limbs and fasciculation (mention the location).
- Muscle power is diminished (mention the location), grades 3/5 and 4/5.
- Knee and ankle jerks are exaggerated, also patellar or ankle clonus (mention, if any).
- Plantar response: Extensor on both sides.
- Sensory is normal.
- Coordination: Difficult to elicit because of weakness.
- Gait: The patient is unable to walk (may be spastic gait).

My diagnosis is **motor neuron disease.**

Remember, for the diagnosis of MND, if any patient presents with:

- Wasting of muscles (weak also).
- But exaggerated reflex.
- No sensory loss and (but fasciculation is present).
- Diagnosis should be motor neuron disease, until proved otherwise.

N.B. During examination, if the patient looks emotionally upset, and there is dribbling of saliva, it is suggestive of pseudobulbar palsy.

Q: What **else** do you like to examine?

A: As follows:

1. Upper limbs: To see signs of LMN lesion in the upper limb (then the diagnosis is amyotrophic lateral sclerosis).
2. Tongue:
 - Wasting and fasciculation (bulbar palsy). Then talk with the patient (nasal voice) and ask about nasal regurgitation.
 - Spastic (pseudobulbar palsy).
3. Jaw jerk (exaggerated in pseudobulbar palsy).
4. Emotionally upset (pseudobulbar palsy).



Wasting in MND



MND (wasting of thenar and hypothenar muscles—claw hand)

Q: What are the **differential diagnoses?**

A: As follows:

1. Diabetes mellitus.
2. Syphilitic amyotrophy or syphilitic cervical pachymeningitis.
3. Paraneoplastic syndrome (commonly due to bronchial carcinoma).
4. Sarcoidosis.
5. Spinal diseases:
 - Cervical cord compression.
 - CASMA (chronic asymmetrical spinal muscular atrophy).
 - Old poliomyelitis (confuses with progressive muscular atrophy).
 - Spinal muscular atrophy of juvenile-onset type-3 (onset in childhood, mild form, affects mostly proximal muscles).
 - Motor neuropathy due to any cause (confuses with progressive muscular atrophy).

Q: Could it be **syringomyelia?**

A: Unlikely, as in syringomyelia there is dissociated sensory loss.

Presentation of Case No. 2: Examination of Hands

(Look at the hands. What are your findings?)

- There is generalized wasting of the small muscles of hands involving the thenar, hypothenar and interossei muscles with dorsal guttering and claw hand [flexion of interphalangeal (IP) joints and extension of metacarpophalangeal (MCP) joints].

Q: Mention **one physical examination** you would like to do. Or, what else do you like to do?

A: I want to see the sensory function. If there is no loss of sensation, my diagnosis is MND. If there is loss of sensation, I have some differential diagnoses:

- Peripheral neuropathy due to any cause.
- Cervical spondylosis.
- Cervical rib.
- Cervical cord compression (neurofibroma and meningioma).
- Leprosy.
- Syringomyelia (dissociated sensory loss and trophic changes in hand).

Q: What are the causes of **wasting of the small muscles of the hand?**

A: As follows:

- MND.
- Syringomyelia.
- Charcot–Marie–Tooth disease.
- Cervical spondylosis.
- Cervical rib.
- Pancoast tumour.
- Following arthritis.
- Peripheral nerve lesion (peripheral neuropathy or combined ulnar and medial nerve lesion).
- Myopathy (dystrophia myotonica).

Q: What **investigations** should be done in this case?

A: No specific test, diagnosis is usually clinical. Investigations are done to exclude other diseases:

- Blood sugar (to exclude diabetic amyotrophy).
- Venereal Disease Research Laboratory (VDRL) test or *Treponema pallidum* haemagglutination (TPHA) to exclude neurosyphilis.
- Chest X-ray (to exclude bronchial carcinoma).
- X-ray of the cervical spine.
- Ultrasonogram of whole abdomen (to see any neoplasm).
- EMG (to confirm fasciculation and denervation).
- Nerve conduction velocity (NCV) (normal motor and sensory conduction).

- Lumbar puncture and CSF study (no abnormality, only slightly raised protein).
- CT or MRI (brain and spinal cord).

N.B. There are certain '*No*'s in MND:

- No sphincter disturbance (rarely involved in late case).
- No sensory involvement.
- No loss of awareness till death.
- No dementia.
- No ocular involvement.
- No cerebellar or extrapyramidal lesion.
- No abnormality of CSF usually.

Read the Following Topics in Relation to MND

Q: What is MND? What are the **causes** of MND?

A: It is a progressive disease of unknown cause, characterized by the degeneration of motor neurons in the spinal cord, cranial nerve nuclei and pyramidal neurons in the motor cortex.

MND is common in middle-aged and elderly, rare before 30 years of age. Males are commonly affected than females (pseudobulbar palsy is more in females). There is no remission and the disease is fatal within 3–5 years. Young patients and those with bulbar symptoms show rapid progression.

Causes are unknown; possible factors are:

- Familial: 5–10% of the cases may be inherited as autosomal dominant.
- May follow viral infection, trauma, exposure to toxin and electric shock.
- Glutamate toxicity has been implicated as a factor in amyotrophic lateral sclerosis (ALS).

Q: What is the **pathology** of MND?

A: Degeneration of Betz cells, pyramidal tract, cranial nerve nuclei and anterior horn cells. Both UMN and LMN may be involved, but there is no sensory involvement.

Q: What are the **types** of MND?

A: According to the site of lesion:

1. Spinal cord lesion:
 - Progressive muscular atrophy (PMA): LMN lesion.
 - Amyotrophic lateral sclerosis (ALS): Combined UMN and LMN (LMN lesion in upper limbs and UMN lesion in lower limbs).
 - Primary lateral sclerosis (PLS): Pure UMN lesion (rare).
2. Cerebral lesion:
 - Progressive bulbar palsy: Medullary lesion.
 - Pseudobulbar palsy: Cortical lesion.

According to type of lesion:

1. Pure UMN lesion: PLS, pseudobulbar palsy.
2. Pure LMN lesion: PMA, bulbar palsy.
3. Mixed lesion: ALS.

Q: How to **treat** MND?

A: As follows:

1. No curative treatment.
2. Supportive treatment:
 - Physical rehabilitation.
 - Psychological support.
 - Occupational rehabilitation.
 - Nutritional care: Change the form and texture of the food, high calorie food supplement, enteral feeding, PEG (percutaneous endoscopic gastrostomy).
 - Speech and communication therapy.
 - Respiratory therapy: NIPPV.
 - Home and hospice care, end-of-life palliative care.
3. Symptomatic treatment:
 - Fatigue: Pyridostigmine, amantadine.
 - Depression: SSRI, venlafaxine, amantadine.
 - Emotional lability: Same.
 - Cramps: Quinine sulphate, vitamin E, clonazepam.
 - Fasciculation: Carbamazepine
 - Spasticity: Baclofen, tizanidine.
 - Sialorrhoea: Hyoscamine sulfate, scopolamine patch.
 - Joint pain: Analgesics, NSAIDs
 - Insomnia: Zolpidem tartrate.
 - Respiratory failure: Bronchodilators.
4. Neuroprotective agents: Riluzole, IGF-1, ASO, vitamin E, Coenzyme Q-10, neuroprotective factors. Riluzole is a glutamate antagonist that may retard progression and prolong the survival.

Q: What is the **prognosis** of MND?

A: MND is a progressive disorder and its remission is unknown. It is usually fatal within 3–5 years. Younger patient with early bulbar syndrome tend to show a more rapid course. Prognosis is relatively better in progressive lateral sclerosis and progressive muscular atrophy.

Q: What is the **cause of death**?

A: Bronchopneumonia, respiratory failure resulting from diaphragmatic paralysis and complication of immobility.

Features and diagnosis of individual MND

Progressive muscular atrophy:

- Weakness, wasting and fasciculation of distal limb muscles, usually starting in small muscles of one or both hands.
- Tendon reflex is lost (due to involvement of anterior horn cell).

Amyotrophic lateral sclerosis:

- Weakness, wasting, fasciculation and loss of all reflexes (LMN lesion) in upper limb **plus** spastic weakness with exaggerated reflexes and extensor plantar response in lower limb (UMN lesion), or commonly there is generalized hyperreflexia.
- Bulbar and pseudobulbar palsy may follow eventually.

Primary lateral sclerosis:

- Only UMN lesion (upper limb and lower limb).
- Progressive tetraparesis with terminal pseudobulbar palsy may occur.

Progressive bulbar palsy:

- Presents with 3 **'Ds'**—dysarthria, dysphonia and dysphagia. There is nasal regurgitation, dribbling of saliva.
- Speech is nasal, indistinct and slurred.
- Tongue: Wasted, wrinkled and fasciculating.
- There is palatal palsy.
- Gag reflex is absent.
- Site of lesion: Nucleus of lower cranial nerves in medulla (IX, X, XI and XII). Lesion is bilateral and LMN type.
- Common causes:
 - Motor neuron disease.
 - Guillain–Barré syndrome.
 - Syringobulbia.
 - Brainstem infarction.
 - Poliomyelitis.
 - Neurosyphilis.
 - Neurosarcoid.

Pseudobulbar palsy:

- This is more common in women.
- Speech: Nasal, slurred, indistinct and high pitched (so called **Donald Duck** or **hot potato** dysarthria due to tight immobile tongue).
- Tongue: Small and tight, spastic, unable to protrude, but no wasting or fasciculation.
- Jaw jerk is exaggerated.
- Palatal movement is absent.
- Gag reflex is present.
- The patient is emotionally labile (crying and laughing).
- Site of lesion: Bilateral UMN lesion (supranuclear) involving the pyramidal tract (supranuclear lesion of lower cranial nerves: IX, X, XI, XII).
- Causes:
 - Bilateral repeated cerebrovascular accident (CVA) involving internal capsule (multi-infarct dementia).
 - Demyelinating disease (MS).
 - Motor neuron disease.

Q: What are the **neurological nonmetastatic syndromes** of malignancy? (Also called paraneoplastic syndrome.)

A: As follows:

- Motor neuron disease.
- Sensory neuropathy.
- Mononeuritis multiplex.
- Cranial polyneuropathy.
- Eaton–Lambert syndrome.
- Spastic paraparesis.
- Cerebellar syndrome.
- Dementia and encephalopathy.
- Progressive multifocal leucoencephalopathy.

Cause of neurological nonmetastatic syndromes is unknown. It may precede the clinical manifestation of malignancy. Usually, it is associated with small-cell carcinoma of the lung and lymphoma.

Q: What is the **difference** between fasciculation and fibrillation of muscle?

A: As follows:

- Fasciculation: Contraction of groups of muscles. It is visible.
- Fibrillation: Contraction of single muscle fibre or unit. It is not visible. Diagnosed by EMG.

Q: What is **fasciculation?** What are the **causes**? What is the **mechanism**?

A: Random spontaneous twitching of a group of muscle fibres or a motor unit that produces movement of the overlying skin or mucous membrane or digits. Fasciculation may be coarse or fine, usually present at rest, but not during voluntary movement. It is usually spontaneous and may be elicited by tapping with finger or hammer over the muscle (this procedure is controversial, as it is not accepted by some neurologists because it should be spontaneous). If fasciculation is present with weakness and wasting, it indicates LMN lesion.

Mechanism of fasciculation: It is due to spontaneous firing of surviving axons that strive to innervate the muscle fibres that have lost their nerve supply.

Causes of fasciculation:

1. Neurogenic:
 - MND.
 - Charcot–Marie–Tooth disease.
 - Spinal muscular atrophy.
 - Radiculopathy (cervical spondylosis, cervical rib).
 - Syringomyelia.
 - Peripheral neuropathy.
 - Creutzfeldt–Jakob disease (CJD)
 - Acute stage of poliomyelitis (rarely in old polio).
 - Syphilitic amyotrophy.
 - Neuralgic amyotrophy.
2. Metabolic:
 - Tetany.
 - Thyrotoxic myopathy.
 - Anticholinergic drugs.
 - OPC poisoning.
3. Normal:
 - Benign fasciculations (in anxiety or tension. It is usually found around the shoulder joint).
 - After exercise in fit adults.
 - After tensilon test
 - Muscle cramps.

Friedreich Ataxia

Usual instructions are:

- Examine the lower limbs. Examine for cerebellar signs in the lower limbs.
- Look at the legs. What are your findings? What else do you want to examine?

Presentation of a Case: Lower Limbs (the Patient is Usually Young)

- The patient has bilateral pes cavus and cocking of toes.
- There is wasting of muscles of leg.
- Muscle tone is diminished in both lower limbs.
- Muscle power is diminished in both lower limbs.
- There is loss of knee and ankle jerks.
- Plantar extensor on both sides.
- Sensory test is normal, but loss of vibration and position senses.
- Coordination is impaired on both lower limbs.
- Ataxic gait (cerebellar).
- Rombergism is positive.

My diagnosis is **Friedreich ataxia.**

Q: What **else** do you want to see?

A: As follows:

- Palate (high arched).
- Spine (kyphoscoliosis).
- Signs of cerebellar lesion (see page 338).
- Eye (nystagmus in 25%, fundoscopy shows optic atrophy in 30%, retinal atrophy and retinitis pigmentosa).
- Heart shows cardiomyopathy (hypertrophic cardiomyopathy, may cause sudden death) and ECG change in 50% cases.
- Sensory neural deafness (in 10% cases).

Q: What are the causes of **high-arched palate?**

A: As follows:

- Friedreich **ataxia.**
- Marfan syndrome.
- Homocystinuria.
- Turner syndrome.
- Tuberous sclerosis.

Q: Why **absent tendon reflex,** but **extensor** plantar response?

A: Because of combination of pyramidal lesion, dorsal column and dorsal root lesion. Also, there is involvement of the peripheral sensory fibres that leads to sensory disturbance in the limbs and depressed tendon reflex.

Q: What are the causes of **pes cavus?**

A: As follows:

- Congenital.
- Friedreich ataxia.
- Charcot–Marie–Tooth disease.
- Hereditary motor and sensory neuropathy.
- Spinocerebellar degeneration.
- Peripheral neuropathy in childhood.

Old poliomyelitis (usually unilateral).

Q: What are the **differential diagnoses** of Friedreich ataxia?

A: As follows:

- MS.
- Tabes dorsalis.
- Spinocerebellar degeneration.

Q: What is **Friedreich ataxia**? What is the **cause**? What are the **features**?

A: It is the most common type of hereditary ataxia inherited as autosomal recessive trait; and in some cases it is inherited as autosomal dominant.

Cause: Unknown. Mutation of *FRDA* gene in chromosome 9. The mutation is abnormal expansion of trinucleotide repeat within a gene that codes for protein 'Frataxin', whose function is to prevent intramitochodrial iron overloading.

Features of Friedreich ataxia are:

- Family history: May be present.
- Usual onset: Young, <15 years (8–16 years).
- Presentations: Progressive difficulty in walking (truncal ataxia and ataxia of lower limbs), weakness of lower limbs and dysarthria.
- Signs are:
 - Cerebellar signs (dysarthria, nystagmus, intention tremor, ataxic gait, etc.).
 - Posterior column: Absent vibration and position sense, positive Rhombergism.
 - Corticospinal tract sign: Plantar extensor, weakness.
 - Peripheral nerve: Absent reflexes in lower limb, wasting of muscles.
- Diabetes mellitus (common).
- Associated with kyphoscoliosis, pes cavus, cocking of toes, optic atrophy, spina bifida and hypertrophic cardiomyopathy (may cause sudden death). Hearing loss.
- Normal mentation (may have mild dementia).
- Prognosis: Usually progresses slowly, death occurs before 40 years of age (usually 20 years after the onset of symptoms due to cardiac and respiratory complications).
- Become chair: Bound 9–15 years after onset of symptoms. May be static and survive up to 60 years.

N.B. In young patients with pes cavus **plus** combination of cerebellar lesion (bilateral), UMN lesion (extensor plantar) and posterior column lesion (loss of vibration and position senses) is highly suggestive of Friedreich ataxia.



Pes cavus

Q: What are the **sites** of lesion in Friedreich ataxia?

A: As follows (there is progressive degeneration):

- Cerebellar lesion.
- Spinocerebellar tract.
- Posterior column lesion (loss of vibration and position sense) and dorsal root ganglia lesion.
- Degeneration of peripheral sensory fibres.
- Corticospinal tract lesion (lateral column lesion).
- Eye (primary optic atrophy).

Q: What are the different **types** of hereditary ataxias?

A: It may be of different types, with different patterns of inheritance:

1. Autosomal recessive:
 - Friedreich ataxia.
 - Ataxia telangiectasia.
 - Ataxia with vitamin E deficiency
2. Autosomal dominant:
 - Spinocerebellar ataxia type 1–28
 - Episodic ataxia
 - DRPLA (Dentatorubropallidoluysian atrophy).
3. X-linked:
 - Fragile X-associated tremor/ataxia syndrome (FXTAS)
4. Mitochondrial:
 - Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS)
 - Myoclonic epilepsy with ragged-red fibres (MERRF)
 - Kearns–Sayre syndrome (KSS)

Q: What are the causes of **combined** cerebellar, pyramidal and dorsal column signs?

A: As follows:

- MS.
- Friedreich ataxia.
- Spinocerebellar degeneration.
- Syphilitic meningomyelitis.
- Arnold–Chiari malformation.

Q: What **investigations** should be done in Freidreich ataxia?

A: As follows:

- CBC, ESR.
- Blood sugar (high in 10%).
- Chest X-ray (cardiomegaly).
- ECG (arrhythmia).
- MRI of brain and spinal cord (shows atrophy of cerebellum and spinal cord).
- NCS (shows that conduction velocity in motor fibres is normal or mildly reduced, but sensory action potentials are small or absent).

Q: How to **manage** this patient?

A: There is no specific therapy. However, the following measures should be taken:

- Physiotherapy and exercise.
- Orthopaedic surgery to correct scoliosis, pes cavus and other deformities.
- Ankle or foot orthoses.
- Walking aids.
- Occupational therapy.
- Visual aids.
- Hearing aids.
- Treatment of related conditions like diabetes mellitus, hypertrophic cardiomyopathy, etc.

Cerebellar Lesion

Usual instructions are:

- Examine for cerebellar signs.
- Talk with the patient. What is your finding? (Scanning speech). What else do you want to examine? (I want to examine to see the cerebellar signs.)

Proceed as follows:

- Look carefully: Head nodding (called **titubation** either **to**-and-**fro** movement—like '**yes–yes**' or rotatory movement like '**no–no**').
- Shoulder is tilted towards the site of lesion (lower down).
- Talk with the patient: Scanning or staccato speech (with bilateral lesion).
- Eye: Nystagmus (jerky, horizontal and coarse with increase in amplitude on looking towards the site of lesion). Skew deviation of the eyes: Ipsilateral down and inwards, and contralateral up and out.
- Finger–nose test: Positive (look for past point and intention tremor that increases on approaching the target).
- Dysdiadochokinesis (rapid alternating pronation and supination of forearm); tap one hand with its palmar, and dorsal aspect on the other hand alternately.
- Rebound phenomenon: Ask the patient to hold both the arms out and front, and keep it. Push both arms and release suddenly. Ipsilateral arm will fly past the starting point (it is due to the failure of reflex arrest).
- Also ask the patient to extend the arms and look for arm drift due to hypotonia of agonist muscles.

Now, examine the **lower limbs** for cerebellar signs:

- Heel–shin test (incoordination).
- Ipsilateral hypotonia (it is due to the loss of facilitatory influence on spinal motor neuron) and diminished muscle power.
- Knee jerk (pendular).
- Dysdiadochokinesis of foot (ask the patient to tap your hand by his/her foot).
- Gait (reeling or drunken: Patient will stagger towards the affected side).

Presentation of a Case

- There is titubation (mention, if any), and tilting of shoulder towards the right or left side.
- Speech is scanning or staccato (jerky, slurred and explosive; the patient talks syllable-by-syllable).
- There is horizontal and coarse nystagmus (right > left).
- Finger–nose test is positive (right, left or both) and intention tremor is present, which is worse as the finger approaches the target.
- Dysdiadochokinesis: Present.
- Heel–shin test: Impaired (incoordination).
- There is hypotonia in the right (or left) lower limb.
- Knee jerk is pendular (mention, if any).
- Gait: Reeling or drunken.
- Rombergism is absent.

My diagnosis is **cerebellar lesion (mention the side—right or left).**

Q: What do you think are the **causes** in this case?

A: Mention the causes according to the age of the patient:

If the patient is young, the causes are:

- Friedreich ataxia.
- MS.
- Wilson disease.
- Drugs (phenytoin and carbamazepine).
- Others: Hypothyroidism and trauma.

If the patient is middle-aged or elderly, the causes are:

- MS.
- Brainstem vascular lesion.
- Paraneoplastic syndrome.
- Alcohol and drugs.
- Secondary deposit in cerebellum.
- Degenerative lesions:
 - Progressive cerebellar degeneration.
 - Olivopontocerebellar degeneration.
 - Shy–Drager syndrome.
 - Creutzfeldt–Jakob disease.

Q: What are the **drugs** causing cerebellar syndrome?
A: Phenytoin, carbamazepine, lithium, phenobarbitone, sometimes chemotherapy agents.

Q: Mention **one investigation** to confirm cerebellar lesion.
A: MRI.

Q: What is the nature of the **cerebellar tremor?**
A: Intension tremor, which is absent at rest but appears during voluntary activity, especially when approaching to a target.

Q: What are the **findings**, if there is **vermis lesion?**
A: As follows:
- Ataxia is usually truncal, causes difficulty in standing and sitting unsupported with broad-based gait.
- Only lower limbs are affected. When limbs are tested separately on bed, usually little or no sign.
- Romberg sign may be positive (same on closing and opening of the eye—to differentiate from sensory ataxia).

Q: What is the **cause** of vermis lesion?
A: Alcohol, which causes atrophy of anterior part of vermis (sparing the upper limb).

Q: When to suspect only **midline lesion**? What are the **causes?**
A: When only truncal ataxia is present, there is abnormal speech and heel–toe walking is positive. The causes are:
- Paraneoplastic syndrome.
- Midline space-occupying lesion.

Q: What are the findings if there is lesion in the cerebellar **hemisphere?**
A: There is ipsilateral limb ataxia.

Read the Following Topics in Relation to Cerebellum

Causes of cerebellar lesion:

1. Vascular [cerebellar haemorrhage or infarction, arteriovenous (AV) malformation and brainstem vascular lesion].
2. Demyelinating (MS).
3. Drugs (phenytoin and carbamazepine) and alcohol.
4. Toxins (carbon monoxide poisoning, solvent abuse and lead poisoning).
5. Neoplasm (haemangioblastoma, medulloblastoma, astrocytoma, secondary deposit and compression by acoustic neuroma).
6. Infection (cerebellar abscess from otitis media, HIV and Kuru).
7. Inherited (Friedreich ataxia and other hereditary ataxias).
8. Cerebellar syndrome of malignancy (paraneoplastic syndrome).
9. Cerebellar syndrome:
 - Shy–Drager syndrome.
 - Steele–Richardson–Olszeweski syndrome.
 - Creutzfeldt–Jakob disease.
 - Wilson disease.
10. Others:
 - Hypothyroidism.
 - Arnold–Chiari lesion.
 - Trauma (punch-drunk syndrome).
 - Cerebral palsy.
 - Hydrocephalus.

Q: What are the **functions** of cerebellum?
A: It is concerned with the control of voluntary movements and maintenance of posture and balance.

Q: What are the malignancies causing **paraneoplastic syndrome of cerebellum?**
A: Carcinoma of ovary, uterus, breast, small-cell carcinoma of the lung, Hodgkin lymphoma, etc. This is probably immune mediated. Cerebellar lesions are usually bilateral (unilateral lesion is against paraneoplastic cerebellar lesion). Two antibodies are recognized for different malignancies:
- Anti-Yo (anti-Purkinje cell antibody): Related to carcinoma of ovary, uterus and breast.
- Anti-Hu (antineuronal cancer antibody): Related to small-cell carcinoma of lung, carcinoma of prostate, sarcoma and neuroblastoma.

N.B. Remember that signs of cerebellar lesion occur on the same side of lesion, because most cerebellar fibres cross twice in brainstem while entering and exiting the cerebellum. **Summary of the signs of cerebellar lesions:**
- Titubation.
- Tilting towards the site of lesion.
- Nystagmus (horizontal).
- Scanning speech.
- Intention tremor.
- Incoordination.
- Dysdiadochokinesis.
- Past-pointing (dysmetria).
- Ataxia.
- Hypotonia.
- Diminished tendon reflex (knee jerk may be pendular).

Parkinsonism

Usual instructions are:

- Look at the face. What are your findings? What else do you want to examine?
- Look at the hands (resting tremor). What else do you want to examine?

Proceed as follows:

1. In the face:
 - Titubation of head.
 - Mask-like, expressionless, less blinking face with staring looks (frequency of spontaneous blinking is reduced, called serpentine stare). Blepharoclonus (tremor of eyelids, when eyes are gently closed).
 - Dribbling of saliva.
2. Talk to the patient: Speech—slow initiation, husky, slurred, indistinct, lacking intonation, low volume and monotonous (or mutism). Palilalia is present (repetition of the end of a word).
3. Glabellar tap: Positive (tap the forehead above the bridge of the nose repeatedly). In normal person, blinking will stop after three to five blinks, but in parkinsonism, the patient continues to blink. This sign is unreliable.
4. Repetitive tapping over the bridge of nose (two per second): Produces a sustained blink response (Myerson sign).
5. Look at the tremor (see below): Present at rest, tremor disappears or reduces with activity or holding something.
6. Rigidity: Lead pipe (better seen in elbow) or cog-wheel (better seen in wrist).
7. Tests for hypokinesia:
 - Ask the patient to do fastening of button.
 - Ask to write (micrographia and handwriting is tremulous and untidy).
 - Ask to touch tip of all fingers with thumb successively or ask to count (slow initiation, unable or can do slowly or progressive reduction of amplitude of each movement).
 - Ask the patient to do rapid fine finger movement (like piano playing): It becomes indistinct, slurred and tremulous.
 - Ask the patient to perform two different simultaneous motor acts (patient is unable to do so).
8. Ask the patient to stand and see the position (flexed and stooped attitude).
9. Gait: Ask to walk and to turn quickly (difficulty in starting to walk, called **freezing,** paucity of movement, less swinging of arms and flexed attitude; inability to turn rapidly, called **fractionated** turn).

Presentation of Case No. 1

(By looking at the face):

- The patient has titubation of head (mention, if any).
- There is mask-like, expressionless face with less blinks of the eyes, staring look and dribbling of saliva.

My diagnosis is **parkinsonism.**

Q: What else do you like to examine?

A: Comment on **resting tremor,** if present. Then tell, "I want to examine the following":

- Glabellar tap (positive).
- Muscle tone (rigidity—cogwheel or lead-pipe).
- Speech (talk to the patient).
- Hypokinesia (see the fastening of button and writing by the patient).
- Gait (see below).

Presentation of Case No. 2

(As described in Case no. 1) plus

- There is resting tremor with pill-rolling movement of right (or left) thumb, which disappears after voluntary movement or holding something.
- Rigidity is present (which is cog wheel or lead pipe).
- There is hypokinesia.
- Speech is husky, slurred, monotonous and low volume.
- Gait (ask the patient to raise from chair, walk, turn quickly, stop and start):
 - Difficulty in starting to walk. Once started, rapid, small, shuffling steps occur (hardly raising the foot from ground), as if trying to keep up with his own centre of gravity.
 - Stooped or flexed attitude with less swinging of arms.
 - Rapid walking and difficulty in stopping himself with tendency to run (festination).
 - He has difficulty in rapid turning (fractionated gait).

My diagnosis is **Parkinsonism.**

Q: What do you think are the **causes** of Parkinsonism in this case?

A: Mention the causes according to the age:

In elderly patients, the causes are:

- Idiopathic or paralytic agitans (the commonest cause).
- Drugs
- Postencephalitic Parkinsonism.
- Neurosyphilis.
- Trauma.
- Cerebral tumour.

In young patients, the causes are:

- Postencephalitic Parkinsonism.
- Drugs.
- Wilson disease.



Face in a case of Parkinsonism



Parkinsonism (flexed attitude)

Q: What specific **past history** would you like to take?

A: As follows:

- History of head injury (punch-drunk syndrome).
- Drugs (phenothiazine, butyrophenone, metochlopramide, reserpine, tetrabenazine, α-methyldopa, lithium, valproic acid, fluoxetine).
- Any history of fever, convulsion, headache, coma (postencephalitic).
- Jaundice, chronic liver disease (CLD) (Wilson disease).
- Any history of headache, vomiting, convulsion (cerebral tumour).

Q: Describe the **tremor** in Parkinsonism.

A: Tremor is involuntary, coarse (4–6 Hz), present at rest, disappears or reduces during voluntary activity and sleep, and increases with emotion or anxiety. Initially, the tremor is characterized by pill-rolling movement between thumb and index finger, flexion and extension of fingers, abduction and adduction of thumb, and pronation and supination of forearm. Later, tremor may affect arms, legs, feet, jaw and tongue. Tremor is absent in one-third cases at presentation and throughout its course in some cases.

Commonly, the patient presents with unilateral resting tremor in hand.

Q: What are the types of **rigidity** in Parkinsonism?

A: They are of two types:

- Lead pipe: Uniform rigidity in flexors and extensors of limbs (better seen in elbow or knee).
- Cog wheel: Rigidity is interrupted by tremor (better seen in wrist joint). It is due to exaggerated stretch reflex interrupted by tremor.

N.B. Sometimes, rigidity of the examining limb is increased with simultaneous active movement of the opposite limb. (It is one type of reinforcement).

Q: What is the **difference** between rigidity and spasticity?

A: As follows:

1. Spasticity means increased resistance during the initial part of passive movement, followed by lessening of the resistance.
 - It may be clasp-knife type, in which there is more resistance at the onset of movement, followed by sudden loss of resistance. It is due to pyramidal lesions. Spasticity is better felt with attempting extension of upper limbs and flexion of lower limbs. It is associated with other signs of UMN lesion. It involves only the antigravity muscles (extensors of the upper limbs and flexors of the lower limbs).
2. Rigidity means sustained uniform resistance during passive movement. Rigidity is found in

extrapyramidal lesion and involves all groups of muscles. It may be:

- Lead pipe in which resistance is uniform throughout the passive movement (better seen in elbow and knee).
- Cog wheel in which continuous resistance is interrupted by tremor (better seen in the wrist and ankle joints).

Q: What are the features of **hysterical rigidity**?

A: In hysterical rigidity, muscle tone increases more and more with increasing manoeuvre of the affected limb. The more the limbs are moved or examined, the more rigid it gets.

Q: What is **dyskinesia or akinesia**? Describe **dyskinesia or hypokinesia** in Parkinsonism.

A: Dyskinesia is the difficulty in initiating motor activity or poverty or slowing of movement (bradykinesia). In Parkinsonism, it may be:

- Difficulty in initiating movement.
- Slowness of movement (bradykinesia). The patient is slow and ineffective in attempt to deliver a quick, hard blow; he cannot complete a rapid ballistic movement.
- Poverty of movement.
- Alternative movement progressively impeded, finally blocked completely.
- Difficulty in executing two motor acts simultaneously.
- Bradykinesia is reflected also by slowness in chewing, limited capacity to make postural adjustment.

Q: What are the **differences** between essential tremor and Parkinsonian tremor?

A: As follows:

Features	Essential tremor	Parkinsonian tremor
Stimulus	Occurs with action	Occurs with rest
Family H/O tremor	Yes	No
Body parts involved	Hands, head	Hands, legs, rarely head
Distribution at onset	Bilateral and symmetric	Unilateral and asymmetric
Sensitivity to alcohol	Yes	No
Course	Stable and slowly progressive	Progressive

Q: Describe the typical **gait** in Parkinsonism.

A: Festinate gait, characterized by:

- Rapid small shuffling step (festination) in order to avoid falling. The patient hardly raises the foot from the ground.
- The patient seems to catch up with his own centre of gravity (flexed attitude).
- There is less swinging of the arms during walking.
- The patient has difficulty in stopping himself.
- He has difficulty in rapid turning (fractionated gait) and turns en block.
- Obstacles cause the patient to freeze in place.

Q: What are the other **abnormal gaits** in Parkinsonism?

A: As follows (these tests should not be done at the bedside):

- Propulsion: If the patient is pushed from behind, he is unable to stop himself and may fall forward.
- Retropulsion: If the patient is pushed from front, he is unable to stop himself and may fall backward.
- Kinesia paradoxica: The patient is unable to initiate a movement; but once started, can complete the whole act (may run down the stairs, but cannot stop at the bottom) or the patient is unable to initiate a movement, but during emotion or fear (e.g. fire in the house), can perform the movement (even run out from the house).

Q: What are the **reflexes and plantar response** in Parkinsonism?

A: All the reflexes and plantar responses are normal. It may be difficult to elicit because of rigidity. Plantar is flexor. It may be extensor if it is associated with the following disorders:

1. Postencephalitic Parkinsonism.
2. Other diseases (called atypical Parkinsonian syndrome):
 - Shy–Drager syndrome
 - Steele–Richardson–Olszeweski syndrome (progressive supranuclear palsy).
 - Olivopontocerebellar atrophy (OPCA)
 - Corticobasal degeneration (CBD).

Q: What is **Parkinsonism?**

A: It is a syndrome consisting of tremor, rigidity, bradykinesia and loss of postural reflexes.

Q: What is **Parkinson disease?**

A: Parkinson disease (paralysis agitans) is the primary or idiopathic Parkinsonism. It is a neurodegenerative disorder due to involvement of the basal ganglia, characterized by slowness of movement, rigidity, tremor and loss of postural reflex.

Q: What is **Parkinsonian plus?**

A: It characterized by features of Parkinsonism with other degenerative disease like progressive supranuclear palsy (Steele–Richardson–Olszeweski syndrome), olivopontocerebellar degeneration, nigrostriatal degeneration, primary autonomic failure (Shy–Drager syndrome).

Features that may indicate a diagnosis of Parkinson-plus syndrome include:

- Symmetrical features, especially at an early stage.
- Early onset of features like postural instability, fall, dementia, hallucinations, autonomic dysfunction, etc.
- Presence of pyramidal signs (not due to previous stroke or other pathology), cerebellar signs or ocular signs (e.g. nystagmus, gaze palsy).
- Poor response to levodopa.

Q: What are the **diagnostic criteria** for Parkinsonism?

A: **Triad** of:

- Tremor at rest (4–6 Hz)
- Rigidity
- Hypokinesia

(Remember the formula **TRH**. According to Brain Bank criteria, postural instability is another criterion).

Q: What is the **pathological change** in Parkinsonism?

A: In idiopathic Parkinsonism, there is progressive degeneration of the pigmented dopaminergic neurons of substantia nigra and formation of eosinophilic cytoplasmic inclusions in neurons (Lewy bodies, which is the pathological hallmark). Hence, there is a deficiency of dopamine (and melanin) with relative increase in cholinergic transmission (imbalance between dopamine and acetylcholine).

Q: What is the **mental status** in a patient with Parkinsonism?

A: As follows:

- Initially, intellect and memory are normal. There may be slowness of thought and memory retrieval (bradyphrenia) and subtle personality changes.
- Depression occurs in one-third of the patients.
- Global dementia (20%) and psychosis.
- Drug treatment may precipitate acute confusion.

Q: What are the **stages** of Parkinsonism?

A: As follows:

- Stage I: Unilateral involvement (hemiplegic Parkinsonism).
- Stage II: Bilateral involvement but no postural abnormality.
- Stage III: Bilateral involvement with mild postural abnormality.
- Stage IV: Stage 3 plus severe postural abnormality requiring substantial help.
- Stage V: Severe, fully developed disease. The patient is restricted to bed and wheel chair.

Q: What are the **causes** of Parkinsonism?

A: Unknown, multiple factors are responsible:

1. Paralysis agitans (idiopathic, also called Parkinson disease). It usually occurs in middle-aged or elderly.
2. Postencephalitic (encephalitis lethargica and Japanese B encephalitis).
3. Drugs: Phenothiazines (chlorpromazine, prochlorperazine), butyrophenones (haloperidol), metoclopramide, sulpiride, cisapride, tetrabenazine and methyldopa.
4. Neurosyphilis.
5. Poisoning: Carbon monoxide, manganese and MPTP (methyl-phenyl-tetrahydropyridine) may occur in drug addicts.
6. Herbicide (paraquat, may be related to MPTP).
7. Trauma (punch-drunk syndrome and repeated head injury).
8. Genetic (Wilson disease and Huntington disease).
9. Cerebral tumour (involving basal ganglia).
10. Parkinsonian plus (when associated with features or pathology of other disease):
 - Shy–Drager syndrome.
 - Steele–Richardson–Olszeweski syndrome (progressive supranuclear palsy, characterized by inability of the movement of eye vertically or laterally and dementia).
 - Olivopontocerebellar degeneration.
11. Creutzfeldt–Jakob disease.
12. Hypoparathyroidism.
13. Normal pressure hydrocephalus (triad of urinary incontinence, gait apraxia and dementia).
14. Atherosclerotic Parkinsonism (stepwise progressive broad-based gait and pyramidal signs).

Q: What **investigations** should be done in Parkinsonism?

A: Diagnosis is usually clinical. Investigations are done for specific cases or to exclude other diseases:

1. CT scan or MRI (may be done if there is pyramidal, cerebellar and autonomic involvement or doubtful diagnosis).
2. In patient <50 years, screening for Wilson disease:
 - Serum ceruloplasmin (low).
 - Serum copper (high serum free copper).

- 24 h urinary copper (high). Following penicillamine therapy, 24 h urinary copper >25 mmol is confirmatory.
- Liver function tests may be done.
- Liver biopsy with quantitative measurement of copper (less done).

Q: How to **differentiate** between postencephalitic Parkinsonism and paralytic agitans?

A: As follows:

Criteria	Postencephalitic	Paralytic agitans
Age	Any, commonly young	Elderly or late-middle age
Onset	Sudden	Insidious
Previous history	Encephalitis, fever and headache	No particular history
Complaints	Mainly rigidity, also impaired higher functions, excess salivation (autonomic features), little or no tremor	Mainly tremor
Symmetry	Fairly symmetrical rigidity and hypokinesia	Asymmetrical
Eye signs:		
• Oculogyric crisis	Present	Absent
• Ophthalmoplegia	Present	Absent
• Pupil	Abnormal (dilated, irregular)	No abnormality
Neurological features:		
• Dystonia, dementia, chorea, hemiparesis	Present	Absent
• Rigidity	Usually lead pipe (due to absence of tremor)	Usually cogwheel
• Tendon reflexes	Brisk	Normal
• Plantar response	Extensor	Flexor
Levodopa	Less sensitive	Sensitive
Prognosis	Not good	Slowly progressive
Lewy body	Absent	Present

Q: What is **oculogyric crisis**?

A: It is an involuntary, sustained upward and outward deviation of the eyes. Causes are:

- Postencephalitic Parkinsonism.
- Drugs (commonly phenothiazines).
- Petit mal epilepsy.

Q: What are the **treatment modalities** in Parkinsonism?

A: As follows:

- Treatment of the cause and withdrawal of offending drugs, if any.
- Symptomatic treatment of tremor, rigidity and bradykinesia.
- Physiotherapy and speech therapy.
- Surgical treatment.
- Occupational therapy and rehabilitation.

Q: What is the **treatment** of Parkinson disease?

A: Drug treatment is usually not started in mild case because of untoward side effects. It should be started when there is significant disability and when the symptoms begin to interfere with work and social life, or falling becomes a threat.

1. Combination of levodopa and dopa decarboxylase inhibitor is the treatment of choice. Available combinations are levodopa and carbidopa (co-careldopa 110 or 275 mg), and levodopa and benserazide (co-beneldopa 62.5 mg). Treatment should be started with lowest possible dose and gradually increased as needed.
2. Tremor and rigidity may be controlled by anticholinergic drugs (such as trihexiphenidyl, benztropine, orphenadrin, benzhexol, biperiden).
3. Other drugs: Amantadine, selegilin, catechol-O-methyl transferase (COMT) inhibitors (entacapone, tolcapone), dopamine agonist (pergolide, bromocriptin, lisuride, ropinirole and pramipexole) may be used.
4. General measures:
 - Physiotherapy and speech therapy.
 - Occupational therapy and rehabilitation.
5. Other measures:
 - Cognitive impairment and psychiatric symptoms may be helped by rivastigmine. (Selective serotonin reuptake inhibitory (SSRI) are drugs of choice for depression. These drugs may aggravate Parkinsonian symptoms. Trazodone is helpful in treating depression and insomnia.)
 - For psychosis, confusion or hallucination: Atypical antipsychotic can be given.

Q: What is the **role of surgery** in Parkinsonism?

A: Surgery may be considered in some particular cases of Parkinson disease. However, it is rarely done because medical treatment is available. Options are:

- Stereotactic thalamotomy (ventrolateral nucleus of thalamus): Usually unilateral. Bilateral thalamotomy is not recommended. It relieves

tremor on the contralateral side (but little effect on bradykinesia, rigidity, motor fluctuation and dyskinesia).

- Pallidotomy: Destruction of a part of the globus pallidus interna is done. It helps in the improvement of contralateral features like tremor, bradykinesia and rigidity. Also reduces dyskinesia. Bilateral pallidotomy is not recommended.
- Subthalamotomy: Involves destruction of a part of subthalamic nucleus. It improves contralateral features like tremor, bradykinesia and rigidity.
- Deep brain stimulation: It is a procedure that has replaced the surgery. A lead is implanted into the targeted brain structure such as thalamus, globus pallidus interna or subthalamic nucleus. Then it is connected to an implantable pulse generator, usually in subclavicular area, that delivers high-frequency electrical discharge. It can be used to stimulate bilateral lesion.
- Foetal midbrain or adrenal tissue implantation in basal ganglia. This is helpful in younger patients. Cannot be used regularly because of ethical issues.

Q: What are **end of dose deterioration** and **on–off phenomenon?**

A: After 3–5 years of levodopa therapy, there may be fluctuating response to levodopa in up to half of the patients. These include:

- **End of dose dyskinesia** (wearing-off effect): Due to progression of the disease and loss of capacity to store dopamine, duration of action of levodopa becomes progressively shorter. As a result, the patient complains of freezing and rigidity before the next dose of levodopa. This may be managed by dividing levodopa into smaller and frequent doses. Also by using slow-release preparations or adding dopamine agonist or adding amantadine.
- **On-off phenomenon**: After prolonged use, the drug may become less effective. There is sudden, unpredictable change in response in which periods of severe Parkinsonism (freezing and immobility—the off period) alternate with periods of dopamine-induced dyskinesias, agitation, chorea and dystonic movements (the on period). This can be managed by lowering the dose of levodopa or adding selegiline with levodopa. COMT inhibitor or dopamine agonist may be added.

Q: What are the **extrapyramidal effects** of phenothiazine group of drugs (or antipsychotic drugs)?

A: As follows:

- Parkinsonism (tremor is less and responds to anticholinergic drugs than L-dopa).
- Dystonia (by prochlorperazine and metoclopramide).
- Akathisia (it is the uncontrolled restlessness with repetitive and irresistible need to move).
- Tardive dyskinesia: Characterized by orofacial dyskinesia including lip smacking, chewing, pouting and grimacing. It is usually due to use of phenothiazines and butyrophenones for at least 6 months. May be worse or may persist after the withdrawal of drug. Tetrabenazine may help.
- Chorea.

Chorea

Usual instructions are:

- Look at the patient. What is your diagnosis? What else do you want to see?

Presentation of a Case (by Looking)

- There is an involuntary, nonrepetitive, quasipurposive, irregular, jerky movement of the arm, head and whole body, which is present at rest and increases after activity.
- The movements are randomly distributed and moves from one part of the body to other.
- The patient looks clumsy and restless (may keep dropping object).
- There may be writhing or dancing movement of the limbs.

My diagnosis is **chorea (or choreoathetosis).**

Q: What **else** do you want to examine?

A: As follows:

- See muscle tone **(**there is **hypotonia).**
- Ask the patient to protrude the tongue: Patient is unable to keep the tongue protruded out. (It darts in and out called serpentine movement or **jack in the box.)**
- Ask the patient to raise both arms above the head opposing the palmar side (hands will **sway outward;** there is pronation of forearm).

- Perform handshake with the patient. (There is alternate squeezing and gripping of patient's finger or lack of sustained hand gripping called **milkmaid's grip.)**
- Ask the patient to raise both arms in front. (There may be flexion of wrist joint and hyperextension of metacarpophalangeal and finger joints called **dinner fork deformity or choreic hand.)**



Chorea



Chorea



Chorea

Q: What **history** should be taken?

A: As follows:

- Family history (in Huntington chorea and Wilson disease).
- Drugs (neuroleptics, phenothiazine, tricyclic antidepressant, oral contraceptive pill, phenytoin and L-dopa).
- In females: Oral contraceptive pill and pregnancy.
- History of encephalitis.
- In young patients or children: History of sore throat or rheumatic fever (rheumatic chorea).
- Others: History of thyrotoxicosis, polycythaemia rubra vera (PRV) and SLE.

Read the following in relation to chorea:

Q: What is **chorea?**

A: It is the involuntary, nonrepetitive, quasipurposive, irregular and jerky movements of one or more parts of the body due to extrapyramidal lesion. Chorea may be unilateral or generalized; sometimes patient attempts to disguise this by completing the involuntary movements with a voluntary movement. It worsens with anxiety or activity and disappears during sleep (chorea—means dance, from a Greek word).

Q: What is the **site of lesion** in chorea?

A: Caudate nucleus of basal ganglia. Also, due to excessive activity in striatum due to dopaminergic drugs used to treat Parkinsonism. Dopaminergic pathways dominate over cholinergic transmission.

Q: What are the **causes** of chorea?

A: As follows:

1. Rheumatic chorea (poststreptococcal called Sydenham chorea or St. Vitus dance).
2. Senile chorea.
3. Hereditary (Huntington chorea, Wilson disease, benign familial chorea, paroxysmal choreoathetosis, spinocerebellar ataxia and neuroacanthocytosis).
4. Drug induced (see above).
5. Pregnancy (called chorea gravidarum).
6. Encephalitis lethargica.
7. Following stroke.
8. Others (rare):
 - Polycythaemia rubra vera and other myeloproliferative disorders.
 - SLE and antiphospholipid syndrome.
 - Endocrine (thyrotoxicosis, idiopathic hypoparathyroidism and hypoglycaemia).
 - Kernicterus.
 - Cerebral birth injury.
 - Cerebral trauma.
 - Creutzfeldt–Jakob disease.

- Henoch–Schönlein purpura.
- Vascular (lacunar infarction and arteriovenous malformation).
- Carbon monoxide poisoning.

Q: How to **treat** chorea?

A: As follows:

- Reassurance and treatment of primary cause (if any).
- Drugs that may be helpful are phenothiazine, butyrophenones (haloperidol), tetrabenazine and sodium valproate.

Q: What is **Sydenham chorea?**

A: It occurs in rheumatic fever due to the involvement of CNS that develops after streptococcal infection and there is diffuse mild encephalitis. History of rheumatic fever may be present in one-third of the cases.

- Common in children and adolescents, more in female, age 5–15 years.
- Chorea is associated with emotional instability, irritability, inattentiveness, confusion and fidgety. Speech is often affected.
- It manifests for long time, may be 6 months after the initial infection.
- Other evidences of rheumatic fever may be absent when chorea is present.
- Carditis may be first manifestation and rheumatic heart disease may occur.
- Fever is unusual, and erythrocyte sedimentation rate (ESR), antistreptolysin O (ASO) titre and C-reactive protein (CRP) are usually normal.
- It is usually self-limiting and recovers within weeks or 1 month (may be 5–15 weeks). Recurrence may occur in 20% cases. Occasionally, it may relapse during pregnancy (called chorea gravidarum) or in those who use oral contraceptive pills.

Treatment:

- No treatment in most cases as recovery is spontaneous.
- In patient with severe chorea: Benzodiazepine, haloperidol, tetrabenazine or valproate may be given.
- Penicillin prophylaxis up to the age of 20 years (as in rheumatic fever).

Q: What is **Huntington chorea?**

A: It is a disorder, inherited as autosomal dominant, in which chorea is associated with progressive dementia. Gene responsible is on the short arm of chromosome 4. Usually present in adult, during the third to fourth decade. Chorea involves lower limb more than upper limb. Occasionally, there is juvenile onset where Parkinsonism is the main feature.

Huntington chorea is **diagnosed** by:

- Family history.
- Chorea followed by progressive dementia, producing a dancing sort of gait.

Other features of Huntington disease, chorea may be associated with the following:

- Bradykinesia.
- Myoclonus.
- Dystonia, dysarthria, dysphasia.
- Ataxia.
- Slow, saccadic eye movements.
- Cognitive impairment.
- Psychiatric disturbance.
- Rigidity.

Pathological changes in Huntington chorea:

- Cerebral atrophy with neuronal loss in caudate nucleus and putamen.

Changes of neurotransmitters:

- Reduction of acetylcholine transferase and glutamic acid decarboxylase (GAD) in the corpus striatum.
- Depletion of γ-aminobutyric acid (GABA), substance P, angiotensin-converting enzyme and metencephalin in substantia nigra.
- High somatostatin level in corpus striatum.

Investigations:

- CT scan or MRI: Atrophy of caudate nucleus and also cerebral atrophy.
- DNA analysis.
- Haloperidol or phenothiazine for dyskinesia. Tetrabenazine may be given.
- Psychological support.
- Institutional care for dementia.
- Genetic counselling is essential.

Q: Name some **involuntary movements.**

A: As follows:

- Tremor.
- Chorea.
- Athetosis.
- Hemiballismus.
- Myoclonus.
- Tic.
- Torsion dystonia (it may be generalized or localized such as spasmodic torticollis, writer's cramp, oromandibular dyskinesia, blepharospasm and hemiplegic dystonia).

Tremor

Usual instructions are:

- Look at this patient. What are your findings (resting tremor)? What else do you want to examine? (See other signs of Parkinsonism.)
- The patient has tremor. Now examine.

Proceed as follows:

1. If the tremor is present at rest, see abduction–adduction of the thumb (pill-rolling movement) and flexion–extension of fingers. Likely diagnosis is **Parkinsonism** (then examine for other signs of Parkinsonism).
2. If no resting tremor, ask the patient to outstretch the hands in front. If tremor is present, it is called **action tremor.** Then examine according to suspicion: Check for thyrotoxicosis, history of taking drugs and family history.
3. If no resting tremor or no tremor with outstretched hands, then test for intention tremor (cerebellar lesion); and if present, check for cerebellar signs.
4. If still no tremor, see for flapping tremor.

Q: What is **tremor?**

A: It is the involuntary, oscillatory and rhythmical movement of one or more parts of the body due to alternate contraction of a group of muscles and their antagonists.

Q: What are the **causes** of tremor?

A: As follows:

- Functional (anxiety, hysterical conversion reaction and nervousness).
- Endocrine (thyrotoxicosis, phaeochromocytoma and hypoglycaemia)
- Parkinsonism.
- Cerebellar tremor (also called intention tremor).
- Benign essential tremor.
- Senile tremor.
- Drugs: Salbutamol and other β-agonist, phenothiazines, butyrophenones, methyldopa, lithium intoxication, anticonvulsant (phenytoin, carbamazepine and sodium valproate), amphetamine, theophylline and caffeine.
- Alcohol (chronic alcoholism and alcohol withdrawal).
- Toxin (mercury, arsenic and lead).
- General paresis of insane (GPI).
- Flapping tremor.

Q: What are the **types** of tremor?

A: They are of three types:

- Resting tremor (typical of Parkinsonism).
- Action tremor or postural tremor (present on outstretched hands).
- Intention tremor.

According to the amplitude or nature, it may be fine or coarse.

Q: What are the causes of **action tremor?**

A: As follows:

- Anxiety.
- Thyrotoxicosis.
- Senile tremor.
- Benign essential tremor.
- Cerebellar tremor (increases near the target).
- Drugs (see above).
- Familial.
- Idiopathic (in many cases).

Q: What is **intention tremor?**

A: Tremor that comes on voluntary movement, but disappears on rest is called intention tremor. It is caused by cerebellar lesion due to any cause.

Q: What are the causes of **fine and coarse tremor?**

A: As follows:

1. Causes of fine tremor:
 - Anxiety or nervousness.
 - Thyrotoxicosis.
 - Senile tremor.
 - Benign essential tremor.
 - Drugs (e.g. salbutamol, terbutaline).
 - Familial.
 - GPI.
2. Causes of coarse tremor:
 - Parkinsonism.
 - Intention tremor.
 - Flapping tremor in hepatic precoma.
 - Wilson disease.
 - Sometimes in senile tremor.

Q: What is the **nature** of tremor of GPI?

A: Tremor is usually present in the tongue, is seen during attempting protrusion, and manifested as backward and forward movement of the tongue called trombone tremor (other features of GPI are dementia, Argyll Robertson pupil and bilateral UMN lesion signs).

Q: What is **benign essential** tremor?

A: It is a familial tremor that is inherited as an autosomal dominant and is usually present in outstretched hands and also when hands adopt a posture such as holding a glass or spoon. Occasionally, present

at rest. Worse in upper limbs. Often, there is titubation. Other features are:

- Slowly progressive, though benign, rarely produces severe disability. No rigidity and no hypokinesia.
- Tremor is not aggravated by movement.
- It is common in elderly (but may occur at any age).
- Handwriting is shaky and untidy, but no micrographia.
- Anxiety increases the tremor.

Site of lesion is patchy neuronal loss in cerebellum and cerebral connection.

Treatment:

- Propranolol is helpful in small dose.
- Alcohol may relieve the tremor; but there is chance of addiction.
- Primidone is sometimes helpful.
- Rarely in severe cases, injection of botulinum toxin may be helpful.
- Rarely, in intractable cases, stereotactic thalamotomy.

Q: What are the **differences** between benign essential tremor and Parkinsonian tremor?

A: (See in 'Parkinsonism').

Speech

Usual instructions are:

1. **Instruction 1:** Talk with the patient or ask some questions (to test whether a candidate can diagnose by talking with the patient). Speech disorders are:
 - Dysphasia.
 - Dysarthria.
 - Dysphonia.
 - Any voice change: Husky and croaky (myxoedema).
2. **Instruction 2** (other than speech disorder): Look at the patient. Now, ask some questions.

 For instruction 1, proceed as follows:
 - Once you talk to the patient, try to find out the nature of speech.
 - Is it dysphasia, dysarthria or dysphonia?

 Next question will be according to the nature of speech, as follows:

 If there is dysarthria, ask some questions to find out type of dysarthria:
 - Try to ask a question with long sentence (e.g. 'Would you please tell me your name and address' ? or 'What breakfast did you take this morning' ?)

 Ask the patient to speak 'British constitution or West Registrar Street.' Ascertain whether the speech is cerebellar or pseudobulbar or bulbar palsy:
 - Is it scanning or staccato? (Slow, slurred, explosive or speech broken into syllable-by-syllable—all suggestive of cerebellar lesion.)
 - Is it spastic? (Pseudobulbar palsy)
 - Is it nasal and indistinct? (Bulbar palsy)

 If there is dysphasia, try to find which type of dysphasia (motor or sensory):
 - See whether comprehension is good (expressive or motor type).
 - Comprehension is impaired (sensory type).

 Ask the following questions:
 - What is your name?

 If unable to answer, then ask:
 - Close your eyes.
 - Put out your tongue.
 - Raise your right or left hand or both hands above head.

 If the patient **can perform** all these, it is **motor type** of dysphasia.

 If comprehension is not good, then ask:
 - What is your name?
 - What is your address?

 The patient answers fluently, but speech is meaningless or incoherent (not related with the question). There may be inappropriate words or new words or nonexisting words. Hence, it is likely to be **sensory type** of dysphasia.

 If the patient **neither answers nor responds** to your instructions, such as:
 - What is your name? (no answer).
 - What is your address? (no answer).

 Then hold a pen. Ask the patient, 'What is it'? If no answer, then ask:
 - 'Is it a key'? The patient answers, 'No'.
 - 'Is it a pen'? The patient answers, 'Yes'.

 Then the diagnosis is **nominal dysphasia** (the patient answers either **yes** or **no).**

Q: What are the **component parts** of speech?

A: There are three component parts of speech:

- Phonation (abnormality is called dysphonia).
- Articulation (abnormality is called dysarthria).
- Language (abnormality is called dysphasia).

Q: What is **dysphasia?**

A: It is the disordered use of language with or without impaired comprehension of received speech.

Q: What are the types of **dysphasia?**

A: As follows:

- Motor dysphasia (expressive).
- Sensory dysphasia (receptive).
- Nominal dysphasia.
- Global dysphasia (both motor and sensory).

N.B. For details about dysphasia, see in the topic "Dysphasia" later in this chapter.

Q: What is **dysarthria?**

A: It means the defect in articulation and enunciation of speech. It may result from the lesion of the muscles, myoneural junctions, or motor neuron of lips, tongue, palate and pharynx.

Q: What are the **types of dysarthria?**

A: As follows:

- Scanning (cerebellar lesion).
- Spastic (pseudobulbar palsy).
- Paralytic (bulbar palsy).
- Extrapyramidal (slow, slurred, monotonous, husky, dysphonia or aphonia).
- Variegated (hypothyroidism, multiple ulcer or thrush in the mouth, amyloidosis due to large tongue and temporomandibular arthritis).

Q: Where are the **sites of lesion** in different types of dysarthria?

A: As follows:

- UMN lesion of cranial nerves.
- Cerebellum.
- Brainstem.
- Extrapyramidal system.
- At the periphery in the muscles of face, lip, tongue and pharynx.

N.B. For details about dysarthria, see in the topic "Dysarthria" later in this chapter.

Q: What is **dysphonia?**

A: It is the alteration of the quality of voice with reduction in volume as a result of vocal cord disease. It is a disorder of vocalization; the fault is in the vocal cord.

Q: What are the **causes of dysphonia?**

A: It is found in laryngitis, tumour of the vocal cord or bilateral adductor paralysis. Sometimes hysterical.

For instruction 2, proceed as follows: There is likely to be obvious diagnosis by looking at the patient. Now talk to the patient to find out typical speech change in that disease. Examples are:

- Hypothyroidism – croaky or husky voice.
- Parkinsonism – slow initiation of voice, dysphonia.

Q: What is the **difference** between dysphasia and dysarthria?

A: Dysphasia is a disorder of language; but dysarthria is a disorder of speech.

Q: Which **cerebral hemisphere** is responsible for language function?

A: The dominant hemisphere. Left hemisphere is dominant in 97% right-handed person and 50–60% left-handed person.

Dysphasia

Usual instructions are:

- Talk with the patient. Or, ask some questions.

Presentation of a Case (Motor Dysphasia): Case No. 1

- The patient can understand, but is unable to talk or answer.
- Or, the patient is unable to talk, but can talk a few words after sometime. There is lack of fluency, has difficulty in finding some words, but comprehension is good.

My diagnosis is **motor (expressive) dysphasia** (also called Broca dysphasia).

Q: What **else** do you want to examine?

A: Hemiplegia, more likely right sided (ask the patient to raise the hands, legs). (In a right-handed person, left hemisphere is dominant; and it is also dominant in 50% of left-handed persons.)

Q: Where is the **site of lesion** in motor dysphasia?

A: Broca area (posterior part of inferior frontal gyrus) in dominant hemisphere (along the middle cerebral artery or of its frontal branch).

Q: What are the **causes**? How is the **prognosis**?

A: Cerebrovascular accident (such as cerebral infarction or haemorrhage). Prognosis is good.

Presentation of a Case (Sensory Dysphasia): Case No. 2

- The patient speaks fluently, but cannot understand the spoken (auditor dysphasia) or written word (alexia).
- Speech is unintelligible, which is incorrect word (hand for foot), inappropriate words (paraphasia, incorrect syllable in word (e.g. tooth brush as tooth smooth), new words (neologism) and nonexisting words (Jargon dysphasia).

My diagnosis is **sensory (receptive) dysphasia.**

Q: What is the **cause**?

A: Cerebrovascular accident (such as infarction or haemorrhage). It may be also due to space-occupying lesion.

Q: Where is the **site of lesion**?

A: Posterior part of dominant superior temporal gyrus (called Wernicke area).

Q: What **else** do you like to examine?

A: As follows:

- Homonymous hemianopia.
- Sensory (impaired or diminished on right side of the body).
- Dyslexia (difficulty in reading).
- Dysgraphia (difficulty in writing).
- Dyscalculia (difficulty in calculation).

Q: What **happens** in repetitive speech?

A: Severely impaired (it is better in expressive type).

Q: What is the **prognosis**?

A: Recovery is usually good.

Presentation of a Case (Nominal Dysphasia): Case No. 3

- The patient has difficulty in naming the object; but comprehension is good and the speech production is relatively good.

My diagnosis is **nominal dysphasia.**

Q: What is **nominal dysphasia**?

A: It is a type of motor dysphasia in which there is difficulty in naming the familiar object (although naming difficulty may occur in all dysphasia), but other aspects of speech are normal. The patient usually talks less, answer is either 'yes' or 'no' and comprehension is good.

Q: Where is the **site of lesion** in nominal dysphasia?

A: Dominant posterior part of the temporoparietal area. It is rare in its pure form. Sometimes, the patient uses long sentences to overcome the failure to find the correct word (circumlocution).

Presentation of a Case (Global Dysphasia): Case No. 4

- The patient has marked disturbance in comprehension and in expression.

My diagnosis is **both motor and sensory (global dysphasia).**

Q: Where is the **site of lesion** in global dysphasia? How is the **prognosis**?

A: Extension of infarction in the left cerebral hemisphere along the territory of left middle cerebral artery. Patient has difficulty in reading, writing and also there is:

- Right-sided hemiplegia.
- Right homonymous hemianopia.
- Marked intellectual deterioration.

Prognosis is **poor**.

Q: What is **conductive** dysphasia?

A: In this type of dysphasia, the patient follows the command, but repeating the statement and naming the object poorly is present.

Q: Where is the **site of lesion**?

A: Arcuate fibre or the fibres communicating between Wernicke and Broca area.

Dysarthria

Usual instructions are:

- Talk with the patient.

Presentation of a Case (Dysarthria): Case No. 1

- The patient has slow, slurred, scanning speech or explosive in nature.

My diagnosis is **cerebellar speech.**

Q: What **else** do you want to see?

A: Cerebellar signs (see cerebellar lesion, page 338.)

Presentation of a Case (Bulbar Palsy): Case No. 2

- The speech is nasal, indistinct, slurred. There is (may be) dribbling of saliva.

My diagnosis is **bulbar palsy.**

N.B. For diagnosis of bulbar palsy, remember the 3 **'Ds'** (Dysarthria, Dysphonia and Dysphagia).

Q: What **else** do you want to see? What is the **site** of lesion in bulbar palsy?

A: As follows:

- Palate: Absent movement (ask the patient to say **'aah'** and see the palate).
- Tongue: Wasting, wrinkled and fasciculation.
- Gag reflex: Absent.
- The patient has nasal regurgitation.

Site of lesion: Nucleus of lower cranial nerves in medulla (IX, X, XI and XII). Lesion is bilateral and LMN type.

Q: What are the **causes of bulbar palsy?**

A: As follows:

- Motor neuron disease.
- Guillain–Barré syndrome.
- Syringobulbia.
- Brainstem infarction.
- Poliomyelitis.
- Neurosyphilis.
- Neurosarcoid.

Presentation of a Case (Pseudobulbar Palsy): Case No. 3

- The speech is indistinct, slurred and high pitched (the so-called **Donald Duck** or **Hot Potato** dysarthria due to tight immobile tongue).
- The tongue is spastic (small and tightened), unable to protrude.
- There is no wasting and no fasciculation.
- Palatal movement is absent.
- Gag reflex is present.
- Jaw jerk is exaggerated.
- The patient is emotionally labile (laughing and crying).

My diagnosis is **pseudobulbar palsy.**

Q: Where is the **site of lesion** in pseudobulbar palsy?

A: Bilateral UMN lesion (supranuclear) involving the pyramidal tract (supranuclear lesion of lower cranial nerves: IX, X, XI, XII).

Q: What **else** do you want to examine?

A: As follows:

- Sensory change (no abnormality).
- Signs of UMN lesion (bilateral generalized spasticity).
- Dysphagia.
- Aphonia or dysphonia (in severe cases).

Q: What are the **causes** of pseudobulbar palsy?

A: As follows:

- Bilateral repeated CVA involving internal capsule (multi-infarct dementia).
- Demyelinating disease (MS).
- Motor neuron disease.
- Others: Brainstem tumour, trauma.

Q: Why pseudobulbar palsy is seen in bilateral lesions only?

A: Because most cranial nerve nuclei receive bilateral innervations from corticobulbar tract.

Q: What are the **differences** between bulbar and pseudobulbar palsy?

A: As follows:

Criteria	Bulbar palsy	Pseudobulbar palsy
Type of lesion	LMN	UMN
Site of lesion	Medulla	Bilateral, internal capsule
Speech	Nasal	Slow, slurred and indistinct
Nasal regurgitation	Present	Absent
Tongue	Wasted, fasciculation	Small, stiff or spastic
Jaw jerk	Absent	Brisk
Emotion	Normal	Labile

Examination of Hands (Wasting of Small Muscles of Hands)

Usual instructions are:

- Look at the hands. What is the diagnosis?
- Examine the hands or examine the upper limb.

By looking, the obvious diagnoses may be possible (for details see 'Examination of Hands' in Chapter 1). In this chapter, wasting of small muscles of hands, related to neurological diseases, are described.

Presentation of a Case (Hand): Case No. 1

- There is generalized wasting of the small muscles of hands involving the thenar, hypothenar and interossei muscles with dorsal guttering and claw hand [flexion of interphalangeal (IP) joints and extension of MCP joints].
- No sensory abnormality.

My diagnosis is **motor neuron disease** (for details, see in MND).

Presentation of Case No. 2

- As in Case no. 1 **plus** sensory abnormality (mention whether median, ulnar or both).

My differential diagnoses are (wasting of small muscles of hand with sensory loss):

- Peripheral neuropathy due to any cause.
- Cervical spondylosis.
- Cervical rib.
- Cervical cord compression (neurofibroma and meningioma).
- Leprosy.

Syringomyelia (dissociated sensory loss and trophic changes in hand).

Q: What **else** do you want to examine?

A: As follows:

- Neck (for cervical spondylosis, cervical rib and supraclavicular bruit).
- Dissociated sensory loss for syringomyelia (for details see page 354).
- Thickening of nerve (at elbow): Leprosy.
- Trophic change, ulcer, gangrene and burn.

Q: What are the **causes** of wasting of small muscles of hand?

A: As follows:

- Motor neuron disease.
- Charcot–Marie–Tooth disease.
- Syringomyelia.
- Cervical spondylosis.
- Cervical cord compression.
- Cervical rib.
- Pancoast tumour.
- Peripheral nerve lesion (polyneuropathy, combined ulnar and median nerve lesion).
- Leprosy.
- RA.
- Myopathy (dystrophia myotonica).

Q: What are the **causes** of wasting in one hand?

A: As follows:

- Cervical cord compression or cervical rib.
- Brachial plexus lesion (trauma and tumour).
- Pancoast tumour.
- Old poliomyelitis.
- Cerebral palsy.
- Leprosy.



Wasting of thenar and hypothenar



Wasting of dorsal interossei guttering

Q: What is **claw hand?** What are the **causes?**

A: It is a deformity of hand characterized by flexion of all interphalangeal (IP) joints and hyperextension of MCP joints. It is due to weakness of the lumbricals and interossei, and unopposed action of long extensors of finger.

Only LMN lesions of C8 and T1 nerves, C8 and T1 nerve root lesion, and brachial plexus lesion will produce localized wasting of lumbricals and interossei causing claw hand. A combined ulnar and median nerve lesion will produce true claw hand. Ulnar claw hand involves fourth and fifth fingers because radial lumbricals are supplied by median nerve.

Causes of claw hand:

- Combined ulnar and median nerve lesion: Trauma, leprosy.
- Brachial plexus lesion (C8 and T1): Cervical rib, thoracic inlet syndrome, Klumpke paralysis.
- Neurological disease: MND, Charcot–Marie–Tooth disease, syringomyelia, intramedullary tumour and polio.

Claw hand-like deformity (pseudoclaw hand) may occur in:

- Dupuytren contracture.
- Volkmann ischaemic contracture.
- Postburn contracture.
- Diabetic cheiroarthropathy.



Claw hand (dorsal surface)



Claw hand (palmar surface)

Syringomyelia

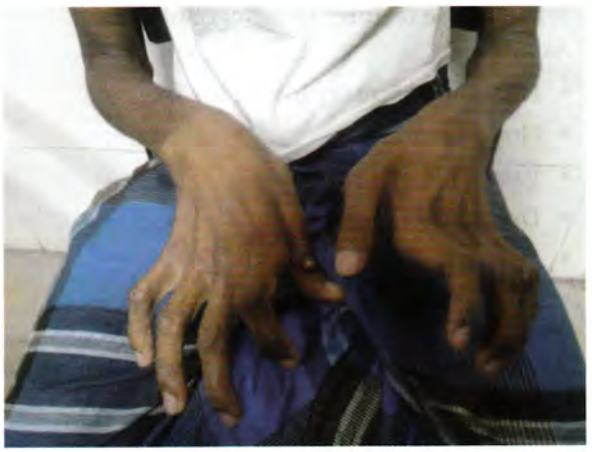
Usual instructions are:

- Examine the hands or perform the neurological examination of the upper limbs (for examination of hands, see in Chapter 1).

Presentation of a Case

- There is a scar mark or burn or painless ulcer on the index finger of right side.
- There is wasting of the small muscles of the hands and forearm; also dorsal guttering of the hands is present. Few fasciculations are present (mention, if any).
- Joints: Hyperextension of MCP and flexion of interphalangeal joints giving rise to claw-hand appearance.
- Muscle tone and muscle power are diminished.
- Biceps, triceps and supinator reflexes are diminished.
- There is dissociated sensory loss (loss of pain and temperature, but intact light touch, vibration and position sense) in the arms, shoulder and neck (classically in 'cape' distribution).

My diagnosis is **syringomyelia.**



Bilateral claw hand and wasting of small muscles of hands in syringomyelia



Hand wasting in syringomyelia

Q: What **else** do you want to examine?

A: As follows:

- Eyes—for Horner syndrome (syringobulbia).
- Kyphoscoliosis, spina bifida and pes cavus.
- Charcot joints of shoulder and elbow.

Examination of lower limbs (may be UMN lesion signs in lower limb, spastic paraplegia).

Q: What is **syringomyelia?**

A: It is a developmental anomaly in which there are cavities filled with fluid surrounded by glial tissue near the centre of spinal cord, mostly originating at C8 and T1 segment, but may occur anywhere in the spinal cord.

Expanding cavity may disrupt:

- Anterior horn cells of spinal cord.
- Lateral spinothalamic tract.
- Corticospinal tract.

May extend upwards to involve the brainstem (syringobulbia).

Q: What are the **causes** of syringomyelia?

A: As follows:

- Developmental anomaly (at the foramen magnum).
- Obstructions of fourth ventricle by congenital defect of the base of the skull or cervical spine (as in Arnold–Chiari malformation).
- There may be arachnoiditis in the region of foramina of Magendie and foramina of Luschka.

Q: How the patient usually **presents?**

A: Presents in third or fourth decade, rarely in early age. The features are:

- Wasting of muscles of hands, forearms, shoulder girdles.
- Loss of pain and temperature sensation. Patient may complain of painless burn.
- Difficulty in walking.

Q: What are the **physical findings** in syringomyelia?

A: Triad of:

- Dissociated sensory loss in neck, shoulder and arm.
- LMN lesion signs in the upper limb (muscle atrophy and loss of reflex).
- UMN lesion signs in lower limbs.



Hand in syringomyelia

Q: What are the **investigations** done?

A: As follows:

- X-ray of the neck (congenital anomaly of foramen and widening of cervical canal).
- MRI (investigation of choice) or CT scan.

Q: What are the **CSF findings?**

A: It may show high protein, which is higher if there is CSF blockage.



Charcot joint in syringomyelia

Q: How to treat syringomyelia?

A: As follows:

- Supportive: Regular activity, physiotherapy; avoid burn, trauma or hot water.
- Surgical decompression may be necessary.

Q: What surgeries are possible?

A: As follows:

- Cervical decompression: In which suboccipital craniectomy, C1–C3 laminectomy and duraplasty. This is done in Arnold-Chiari malformation.
- Dorsolateral myelotomy: In which syrinx is drained into the subarachnoid space, usually done following decompression.
- Shunt: Such as syringoperitoneal shunt, syringosubarachnoid shunt, ventriculoperitoneal shunt.

Q: What are the features of syringobulbia?

A: As follows:

- Dissociated sensory loss in the face.
- Horner syndrome.
- Palatal palsy.
- Dysarthria.
- Nystagmus.
- Cranial nerve involvement (V, VII, IX and X).

Q: What is dissociated sensory loss? What are the causes?

A: Loss of pain and temperature, but intact light touch, vibration and position sense.

Causes of dissociated sensory loss:

1. Lesion at the centre of spinal cord (sensory loss is always bilateral and segmental). The causes are:
 - Syringomyelia (the commonest).
 - Intramedullary neoplasm of the spinal cord.
 - Haematomyelia.
2. Hemisection of spinal cord (Brown–Séquard syndrome).
3. Lesion at the anterior half of the spinal cord: Anterior spinal artery occlusion (LMN lesion at the site, and bilateral UMN lesion and lateral spinothalamic lesion below).
4. Lateral medullary syndrome: Thrombosis of posterior inferior cerebellar artery (PICA). Syringobulbia also produces same type of lesion.

Myotonic Dystrophy

Usual instructions are:

- Examine the hands. What else do you want to see?
- Look at the patient. What is your diagnosis? What else do you want to see?

Proceed as follows (first instruction):

- Look at the hands: Front and back (apparently no abnormality).
- Tell the patient, 'Close and open your hands repeatedly as quickly as possible.' The patient is unable to open the closed hands **(myotonia).**
- Shake hands with the patient (unable to relax the hands—**grip myotonia).**
- Percuss on thenar eminence with your fingers. There are dimples or depressions that fill up slowly **(percussion myotonia).**
- Look at the face of the patient (signs in face—see below).
- Percussion may be done on the tongue (dimples or depressions are seen).

Presentation of a Case (Hands): Case No. 1

- The patient has myotonia, as suggested by the inability to open the hands after closing and also to relax the hands after handshaking.
- There are also dimples on the percussion of thenar eminence.

My diagnosis is **myotonia.**



Myotonia



Myotonia dystrophica

Q: What is **myotonia?**

A: It is the continued contraction of the muscles after cessation of voluntary contraction.

Q: What is **myotonia congenita?**

A: It is an inherited disorder (autosomal dominant) that is characterized by failure to relax the muscle after forceful contraction. Present at birth with feeding difficulty, inability to open the eyes and a peculiar cry. It is a mild disease that improves with age. Other features of myotonia dystrophica are absent. There may be diffuse muscular hypertrophy due to continuous involuntary isometric contraction.

Prognosis: Normal life expectancy.

Treatment: Procainamide or quinidine may be helpful.

Presentation of a Case (by Looking at Face and Other Parts): Case No. 2

1. In face:
 - Frontal baldness (patient may be wearing wig).
 - Long, lean, triangular, sad and expressionless face.
 - Wasting of temporalis and masseter.
2. Eyes:
 - Partial ptosis (usually bilateral, may be unilateral) with smooth forehead.
 - Cataract (stellate cataract). May be posterior subcapsular fine deposit.
 - Difficulty in opening the eyes after firm closure.
3. Neck: Wasting of sternomastoid and shoulder girdle muscles. There is weakness of flexion and normal extension.
4. Others:
 - Wasting of distal muscles of arms (forearm wasting first) and legs.
 - Testes (atrophy).
 - Gynaecomastia.

My diagnosis is **myotonic dystrophy.**

Q: What are the **other features** of myotonia dystrophica?

A: As follows:

- Inherited as autosomal dominant.
- Males are affected more than females.
- Age of onset may be any.
- Diabetes mellitus and impaired glucose tolerance (IGT) may occur.
- Intellect and personality may have mild deterioration.
- Small pituitary fossa and hypogonadism may occur.
- Low serum IgG levels.

Tolerate anaesthesia poorly.

Heart (cardiomyopathy, valvular heart disease, mitral valve prolapsed, and arrhythmia or conduction defect).

Q: What do you mean by **myopathic facies?**

A: It is characterized by expressionless, sad-like facies with frontal baldness and ptosis. Sometimes looks like sleepy appearance.

Q: What is the **gait** in myotonic dystrophy?
A: There is high steppage gait. Foot drop is present.

Q: What are the **types** of myotonic dystrophy?
A: They are of two types:

- Type 1: Classical type associated with distal muscular wasting and weakness.
- Type 2: Similar features, but there is proximal wasting and weakness.

Q: What are the **EMG findings**?
A: High-frequency activity that varies repeatedly to cause a characteristic sound on loud speaker (waxing and waning of potentials called **Dive-Bomber effect).**

Q: How to **treat** myotonia dystrophica?
A: Only symptomatic. No specific treatment.

- Myotonia may be treated by phenytoin (procainamide or quinidine may be used, but may worsen cardiac conduction).
- Genetic counselling.

Q: What are the **causes of myotonia?**
A: As follows:

- Myotonia dystrophica.
- Myotonia congenita.
- Others: Hyperkalaemic periodic paralysis, myxoedema (Hoffman syndrome), hereditary paramyotonia (autosomal dominant), cold-induced myotonia and drug (clofibrate).

Myopathy (Muscular Dystrophy)

Usual instructions are:

- Examine the upper limbs or lower limbs.
- Look at the face. What are your findings? Examine the relevants.

Presentation of a Case (Limb–Girdle Myopathy): Case No. 1

- There is wasting of muscles of both upper limbs with muscular weakness, mainly involving the proximal (proximal myopathy).
- Muscle tone is normal. Reflexes are normal or slightly reduced.
- No sensory abnormality.

My diagnosis is **limb–girdle myopathy.**



Limb–girdle myopathy (front)



Limb–girdle myopathy (back)

Q: What **else** do you want to see?
A: I want to examine the lower limbs (findings like upper limbs).

Q: What is **limb–girdle myopathy**?
A: It is a type of muscular dystrophy characterized by the involvement of shoulder and pelvic girdle muscles.

- Type 1 (10%): Autosomal dominant; slower and later onset.
- Type 2 (90%): Autosomal recessive; occurs in childhood or early adulthood.
- Age of onset is 10–30 years; male and female are equally affected.
- May involve cardiac muscle (may cause conduction abnormality or heart failure).
- Calf pseudohypertrophy sometimes occurs.
- Face and hands are spared.

- Intelligence is normal.
- Muscle enzymes are normal or slightly elevated.
- Prognosis is poor; chair-bound at 20–25 years of age (10–20 years after the onset of disease).

Presentation of a Case (Fascio–Scapulo–Humeral Dystrophy): Case No. 2

- There is wasting of muscles of face, neck and shoulder girdle.
- Face looks dull, expressionless; lips open and slack; inability to whistle and puff the cheek.
- Eyes: Bilateral partial ptosis.
- Winging of scapula (due to the involvement of serratus anterior muscle).
- Pectoralis and trapezius are also wasted.

My diagnosis is **fascio–scapulo–humeral dystrophy**.



Fascio–scapulo–humeral dystrophy



Pseudohypertrophy of calf muscles

Q: What is fascio–scapulo–humeral dystrophy? What are the features?

A: It is a type of muscular dystrophy that is inherited as an autosomal dominant, which is characterized by the involvement of muscles of the face and shoulder girdle.

- Onset is 10–40 years of age.
- Course is variable, but usually relatively benign.
- There is wasting of muscles of face, neck and shoulder girdle (lower trapezzi, pectoralis, biceps, triceps). Hypertrophy of the deltoid.
- Winging of scapula (due to the involvement of serratus anterior muscle).
- Pain in shoulder girdle is common.
- Face looks dull, expressionless; lips open and slack; inability to whistle and puff the cheek.
- Eyes: Bilateral partial ptosis.
- There may be distal lower-limb weakness.
- Lower abdominal muscles are specifically involved with sparing of upper abdominal muscles (Beevor sign—ask the patient to lie flat; then ask him to raise the head. This results in contraction of the upper abdominal muscles, with displacement of the umbilicus upwards).
- Lower limb muscles are affected in 50% cases, which usually affects at later age. Then foot drop occurs.
- Fundoscopy: Retinal telangiectasia in 60% cases.
- Intelligence is normal.
- Prognosis: Normal life span and slowly progressive.
- Muscle enzymes are usually normal or slightly elevated.
- Inflammatory and perivascular inflammation may be seen in muscle biopsy. Also, retinal microvascular abnormality may be found.

Presentation of a Case (Becker Muscular Dystrophy): Case No. 3

(Male young)

- There is pseudohypertrophy of calf muscles (also deltoid, muscles of buttock and infraspinatus).
- Proximal myopathy is present, mainly lower limb (face is normal).

My diagnosis is **Becker muscular dystrophy**.

Q: What is Becker muscular dystrophy?

A: It is inherited as X-linked disorder, only males are affected and features are same as Duchenne type with the exception of:

- Onset is late (5–25 years).
- Less severe, less rapid progression and less cardiomyopathy. Mental retardation and kyphoscoliosis are uncommon. Respiratory involvement is a late feature.
- Chair bound at about 25 years after the onset.
- Survival up to fourth to fifth decade.

Causes of **pseudohypertrophy** of calf muscles:

- Duchenne muscular dystrophy.
- Becker muscular dystrophy.

Q: What is **Duchenne muscular dystrophy?** What are the **features?**

A: It is inherited as X-linked recessive disorder (30% spontaneous mutation). Duchenne gene is on the short arm of X-chromosome, Xp21; and its product called dystrophin is absent (diagnosed by western blot analysis of muscle biopsy).

- Affects only male, age of onset is 3–4 years.
- The child presents with difficulty in walking or getting up from sitting or lying position. There is history of frequent fall and delayed motor activity (e.g. walking).
- Gower sign is positive (while the child gets up from lying position, he uses the hands to climb up).
- There is pseudohypertrophy in early stage involving calf and deltoid muscles. Later there is weakness; it first involves the proximal muscles.
- Gait: Waddling (duck like).
- Other features include dilated cardiomyopathy, kyphoscoliosis and mental retardation. There is early respiratory involvement.
- Prognosis is poor, chair bound by the age of 10 years and few survive up to 20 years.
- Causes of death are dilated cardiomyopathy and respiratory failure or inanition.

Q: What is **myopathy?**

A: It means disease of the skeletal muscle (voluntary) muscle.

Q: What is **muscular dystrophy?** What are the **types** of muscular dystrophy?

A: It is a group of hereditary muscular disorder characterized by progressive degeneration of groups of muscles without the involvement of nervous system with absence or reduced dystrophin. The types are:

1. Hereditary muscular dystrophy:
 - Duchenne type (pseudohypertrophic).
 - Becker muscular dystrophy.
 - Limb–girdle myopathy.
 - Fascio–scapulo–humeral dystrophy.
 - Myotonia dystrophica.
 - Myotonia congenita.
 - Others are oculopharyngeal or ocular myopathy, and congenital muscular dystrophy.
2. Congenital myopathy (rare):
 - Central core.
 - Nemaline myopathy.
 - Myotubular myopathy.
3. Secondary myopathy (endocrine disease and drugs).

Q: What are the **differences** between neuropathy and myopathy?

A: As follows:

- Myopathy usually involves proximal muscles (except myotonia dystrophica, which involves distal muscles).
- Neuropathy usually involves distal muscles (except diabetic amyotrophy), GBS, amyloidosis, Lyme disease.

Q: What **investigations** should be done in myopathy?

A: As follows:

- Creatine phosphokinase (CPK) is very high, up to 40-fold in Duchenne type (in other types, slightly raised).
- EMG shows short duration, low amplitude, spiky polyphasic action potential (spontaneous fibrillation is also seen occasionally), reduction in motor unit amplitude and duration with normal number of units activated during effort.
- ECG (cardiomyopathy and dysrhythmia), echocardiography, blood sugar.
- Muscle biopsy (shows variation of muscle fibre size, degenerative changes, regeneration and replacement by fat. On immunological staining, there is absence of dystrophin. This is commonly found in Duchenne muscular dystrophy).
- Lactic acid (to exclude mitochondrial myopathy).
- Molecular genetic testing.

Carpal Tunnel Syndrome

Usual instructions are:

- Examine the hands or look at the hands. What are your findings?

Proceed as follows:

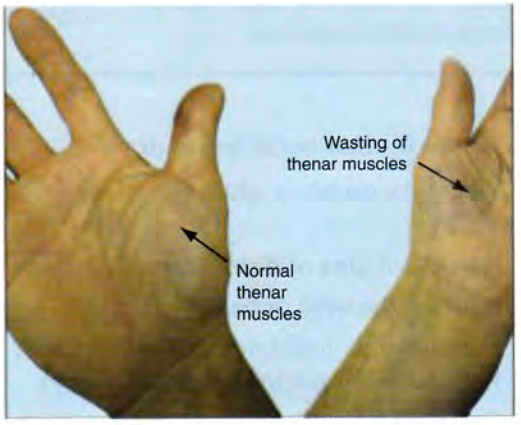
1. Look at palm (wasting of thenar muscles).
2. Perform sensory test (loss of sensation along lateral three-and-half fingers).
3. Motor functions: Examine the thumb (weakness of abduction, flexion and opposition of thumb) and also examine for interossei (Chapter 1).
 - Pen touching test (to assess for the weakness of abductor pollicis brevis): Ask the patient to lay the hand flat with palm upward. Ask to abduct the thumb vertically to touch the pen held above it. It is impossible, if median nerve palsy.

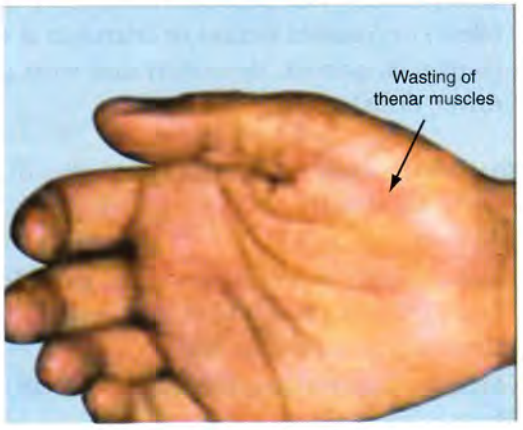
4. Elicit the following signs:
 - Tinel sign: Percussion over the flexor aspect of the wrist (flexor retinaculum) or tap the median nerve in forearm, the patient may experience paraesthesia along the distribution of the nerve.
 - Phalen sign: Flexion or extension of the wrist for 1 min produces paraesthesia along the distribution of nerve (lateral three-and-half fingers).
 - Tourniquet test: Raise BP above systolic for 2 min (produces paraesthesia).
 - Durkan test: Direct pressure over carpal tunnel for 30 s may produce paraesthesia.
 - Closed fist test: Flexion of the fingers into a closed fist for 60 s produce paraesthesia in the median nerve distribution.

Presentation of a Case

- There is wasting of thenar muscles.
- Weakness of abduction, flexion and opposition of thumb, and weakness of lateral two lumbricals.
- Loss of sensation along the radial three-and-half fingers.

My diagnosis is **carpal tunnel syndrome.**





Carpal tunnel syndrome

Q: What **else** do you want to see?

A: I want to see the evidence of primary cause (see below).

Q: What are the nerves involved in **entrapment neuropathy?**

A: As follows:
- Median nerve (at wrist).
- Ulnar nerve (at elbow or at wrist in Guyon canal—bounded proximally by pisiform bone and distally by the hook of the hammet).
- Radial nerve (at spiral groove of humerus following fracture).
- Meralgia paraesthetica (at inguinal ligament).
- Common peroneal nerve or lateral popliteal nerve (at the neck of fibula).

Tarsal tunnel syndrome (at the flexor retinaculum at ankle joint, there is compression of posterior tibial nerve).

N.B. In entrapment neuropathy, there is demyelination, may be axonal degeneration.

Q: What is **carpal tunnel syndrome?** What are the **causes?**

A: It is a type of entrapment neuropathy due to compression of median nerve under flexor retinaculum of wrist causing wasting, tingling, numbness and pain along the distribution of nerve. It is more common in female, less in male.

Causes of carpal tunnel syndrome
- Pregnancy (due to fluid retention, usually in the third trimester).
- Obesity.
- RA.
- Acromegaly.
- Myxoedema.
- CRF on long-term dialysis (due to deposition of β2-microglobulin—an amyloid).
- Tuberculous tenosynovitis.
- Primary amyloidosis.
- Tophaceous gout.
- Drug (oral contraceptive pill).
- Osteoarthrosis of carpus (related to old fracture).
- Idiopathic (common in female, middle-aged and obese. May occur in male with unaccustomed hand use, e.g. house painting).

Q: What is the **usual presentation** of carpal tunnel syndrome?

A: Nocturnal pain, numbness, and paraesthesia in palm and fingers often occurs at night, awakening the patient from sleep. Pain may be referred to whole arm and shoulder.

Q: How to confirm the **diagnosis?**

A: By nerve conduction study.

Q: How to **treat?**

A: As follows:

- Treatment of primary cause.
- Splint in wrist, especially at night; local steroid injection (in intracarpal tunnel) and diuretic may help.

In severe cases: Surgical decompression of carpal tunnel may be required.

Q: What is **meralgia paraesthetica?**

A: It is a type of entrapment neuropathy due to the compression of lateral cutaneous nerve of thigh on leaving the pelvis, just medial to the anterior superior iliac spine. There is pain and paraesthesia over the upper and outer thigh, with reduction of sensation. It is usually self-limiting. Occasionally, may be treated with corticosteroid and local anaesthetic injection at the anterior superior iliac spine. Causes are:

- Obesity.
- Pregnancy.
- DM.
- Idiopathic.
- May be tight jeans.

Muscles supplied by median nerve, mnemonic: LOAF

- **L:** Lateral two lumbricals.
- **O:** Opponens pollicis.
- **A:** Abductor pollicis brevis.
- **F:** Flexor pollicis brevis.

Ulnar Nerve Palsy

Usual instructions are:

- Examine the hands or look at the hands. What are your findings? What else do you want to do?

Proceed as follows:

1. Look at palmar and dorsal aspect of hands. If generalized wasting, perform the neurological examination of hands (Chapter 1).
2. To find out causes:
 - Evidence of fracture or dislocation of the elbow (injury, any scar or deformity).
 - Evidence of osteoarthrosis at elbow.
 - Injury at the wrist or palm.
 - Thickened nerve.
 - Any causes of mononeuritis multiplex.

Presentation of a Case

- There is generalized wasting of the small muscles of hands (except thenar) with dorsal guttering.
- Ulnar claw hand (extension of MCP and flexion of IP joint of fifth and fourth fingers).
- Loss of sensation along fifth and half of the fourth finger.
- There is weakness of abduction and adduction of fingers.
- There is also wasting of the medial side of forearm (due to involvement of flexor carpi ulnaris and medial half of flexor digitorum profundus).
- Froment sign is positive.

My diagnosis is **ulnar nerve lesion or palsy.**

Q: What are the **causes** of ulnar nerve lesion?

A: As follows:

- Fracture of ulna or dislocation of elbow.
- Injury at the wrist or palm.
- Mononeuritis multiplex due to any cause (DM, PAN, RA, SLE, amyloidosis and leprosy).
- Osteoarthrosis of elbow.
- Occupation: With constant leaning of elbows (clerk) or constant flexion or extension at elbow (carpenter, painter, decorator) and wrist (screw driver, drills).

Q: What are the **motor and sensory** supplies of ulnar nerve (C8 and T1)?

A: As follows:

- Motor supply to small muscles of hand (except LOAF), flexor carpi ulnaris and medial half of flexor digitorum profundus.
- Sensory supply to the fifth finger and half of the fourth finger.

Radial Nerve Palsy

Usual instructions are:

- Examine the hands or look at the hands. What are your findings? What else do you want to do?

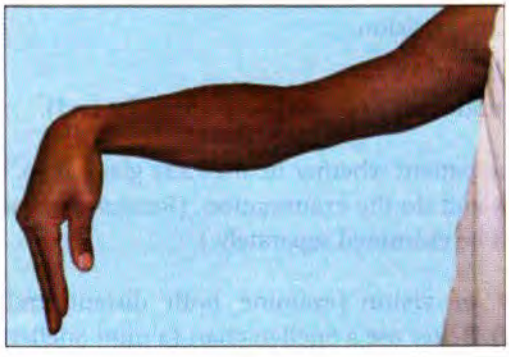
Proceed as follows:

1. Ask the patient:
 - To raise both arms in front (obvious wrist drop).
 - To extend the wrist (weakness of wrist extension).
 - To extend the elbow against resistance; weakness of elbow extension (triceps involvement).
2. Test for brachioradialis: Ask to flex the elbow with forearm halfway between pronation and supination (failure to flex; brachioradialis does not spring up).
3. Pronation and supination (impaired).
4. The patient is unable to straighten the fingers. However, if the wrist is passively extended, the patient is able to straighten fingers at IP joints (due to action of interossei and lumbricals), but is unable to extend MCP joints.
5. Grasp is weak, but grip improves if wrist is extended.
6. Check sensation over the anatomical snuff box for dorsal aspect of thumb (there is loss of sensation).
7. Triceps reflex (absent).

Q: What are the **causes of radial nerve palsy?**

A: According to the site:

- Axilla: Trauma, radiation, compression by improper use of crutch, axillary growth.
- Spiral groove or mid-shaft of the humerus: Trauma, compression (e.g. saturday night palsy).
- Proximal forearm: Trauma, subluxation of the radius, repetitive forearm supination.
- Wrist: Trauma, compression by tight bracelet or handcuff.
- Chronic lead poisoning.
- Mononeuritis multiplex (due to any cause).



Wrist drop

Q: What is **Saturday night palsy?**

A: In this disorder, the patient is heavily sedated with alcohol, sleeps with the arms hanging over the back of chair and radial nerve is compressed at the middle-third of the humerus causing paralysis of the nerve. Brachioradialis, supinator and extensors of forearm are involved. Usually, complete recovery occurs within weeks.

N.B. Radial nerve is vulnerable to be involved at three sites:

- Axilla (incorrect use of crutch).
- Spiral groove of humerus (mid-shaft fracture and saturday night palsy).
- Damage to the posterior interosseous nerve at proximal forearm, where it penetrates the supinator muscle.
- Sensory branch may be compressed at the wrist.

Anatomy of the radial nerve: It is the termination of the posterior cord of brachial plexus, derived from the C5–8 and T1 spinal nerve. In elbow, it gives two branches—superficial radial (entirely sensory) and posterior interosseous (entirely muscular). It gives motor supply to brachioradialis, supinator and extensors of the forearm.

Cranial Nerves

Usual instructions are:

- Examine the cranial nerves.
 (Remember, the examiner may stop you at any point and you must be ready to answer.)

Proceed as follows:

- Ask the patient to sit at the edge of bed, face-to-face. See any obvious finding (ptosis, squint, asymmetry of face and dribbling of saliva).
- Now examine the individual cranial nerve as follows:

First Cranial Nerve

- Examine the nose quickly with a torch light to see any deviated nasal septum (DNS), polyp.
- Ask the patient, 'Do you have any difficulty in your sense of smell'?
 (Ideally use a perfume, put in each nostril and ask, 'Do you get the smell'?)

Second Cranial Nerve

- Acuity of vision.
- Colour vision.
- Field of vision.
- Fundoscopy (should be done at the end).

Ask the patient whether he uses any glass. If so, ask to wear it and do the examination. (Remember, each eye should be examined separately.)

Acuity of vision (examine both distant and near vision): Better use a Snellen chart (a mini Snellen chart may be used). If not available, proceed as follows:

- Distant vision: Ask the patient, 'Look at the wall clock. What is the time now' ? '"Look at the window. How many rods are there in the window' ?
- Near vision: Ask, 'Read the newspaper or any small object'.

Colour vision (ideally it should be done with Ishihara chart):

- Show different colours to the patient and ask, 'What colour is it'?

Field of vision (Sit opposite to the patient, 1-m apart at a same plane. Test each eye separately):

- To examine the right eye, ask the patient, 'Cover your left eye with left hand gently, look steadily at my left eye' (you should cover your right eye). No one should move the eye and should look each other's tip of the nose.
- Hold your index finger midway and from periphery, bring towards the centre until you see it. Ask the patient, 'Do you see my finger? Tell me when you see it.'
- If the patient fails to see, continue to bring the finger and ask when the patient can see.
- In this way, see in horizontal, upper and lower quadrant (temporal field).
- Then, see nasal field in the same way.
- Change your hand and repeat in other eye in the same manner.

Test of central scotoma:

- Use a red-headed pin; move it from temporal side to nasal side in the midway. Ask the patient, 'Do you see it? Tell me, when it disappears'.

Finally perform fundoscopy (see in Chapter 10, 'Examination of the Eye')

IIIrd, IVth and VIth Cranial Nerves

- Look for any obvious ptosis and squint. Next examine eye movement.
- Ask the patient, 'Look at my finger. Follow it with your eyes with head fixed'.
- See movements in horizontal and vertical directions like the pattern 'H'.
- See **nystagmus.** At extreme gaze, ask, 'Do you see one or two fingers (diplopia)'?
- Next examine pupil: Size, shape, light and accommodation reflex (see in Chapter 10, 'Examination of the Eye').

If diplopia is present, further test is necessary as follows:

- Ask to describe false image (it is pale, less distinct and more peripheral than real one). Ask, 'Whether two images lie side-by-side or one above the other'.
- If images are side-by-side, it indicates medial or lateral rectus palsy. If images lie on one above the other, then either oblique muscles or superior or inferior recti are involved.
- To decide which pair of muscles are responsible, ask, 'In which direction, there is maximum image separation?'" (Separation is greatest in the direction in which the weak muscle has its purest action.)
- Now at the point of maximum separation, cover one eye and find which image disappears. Loss of lateral image indicates that covered eye is responsible.
- If diplopia persists after covering one eye, it may be due to astigmatism, dislocated lens or conversion disorder.

Vth Cranial Nerve

Perform both motor and sensory tests:

Motor test (see any wasting of masseter and temporalis muscles):

- Ask the patient, 'Clench your teeth tightly.' Palpate the muscles.
- Test for pterygoids: Ask the patient, 'Open your mouth and stop me from closing it'. (If paralysis is on one side, muscle of that side is less prominent and jaw deviates towards the side of lesion.)
- Test for jaw jerk.

Sensory test: Test along the three divisions of nerve on each side using cotton and pin with eye closed.

Test corneal reflex with wisp of cotton. Touch the cornea (not conjunctiva); see if there is reflex blinking.

N.B. Remember the following points:

- Corneal reflex: Afferent (sensory) passes through ophthalmic division of Vth nerve and efferent (motor) through VIIth nerve.
- If blinking on contralateral eye, but absent in tested eye, it indicates VIIth nerve lesion in ipsilateral eye (eye tested). Only one or three divisions of Vth nerve may be lost:
 - If all sensory are lost, then lesion in ganglia or sensory root (acoustic neuroma).
 - If only one branch of sensory is lost, then lesion is preganglionic.
 - If dissociated sensory loss in face, then lesion in brainstem or upper cervical cord (occlusion of posterior inferior cerebellar artery).

VIIth Cranial Nerve

Perform both motor and sensory tests: Look at the face and see the following (present in VIIth nerve palsy)

- Obvious facial asymmetry; and the affected eye appears open and wide.
- Unilateral drooping of the corners of mouth.
- Nasolabial fold is less pronounced.

Motor test:

- Tell the patient, Look at the ceiling, keep head fixed' . See wrinkling of forehead—unilateral or bilateral (frontal belly of occipitofrontalis).
- 'Close your eyes tightly; do not let me open' (orbicularis oculi). If fails to close, look for Bell phenomenon.
- 'Ask to whistle' (orbicularis oris).
- 'Puff your cheek out' (buccinator). If paralysis, air escapes easily on the affected side.
- 'Show me your teeth and have a smile' (levator anguli oris and risorius). If paralysis is present, face is drawn to the healthy side.

Sensory test:

- Taste sensation in anterior two-thirds of the tongue (nerve fibres pass along the lingual nerve to chorda tympani, then to geniculate ganglion of facial nerve and then to medulla oblongata).
- Posterior one-third of tongue is through glossopharyngeal nerve.

Finally, look at external auditory meatus and palate to see rash (Ramsay Hunt syndrome). Also, test for hyperacusis (nerve to the stapedius muscle).

VIIIth Cranial Nerve

Vestibular division:

- Ask the patient about any vertigo or dizziness or giddiness.

Cochlear division:

- Look at the external ear and meatus (wax and rash).
- Rub your finger or keep watch near ear, ask the patient, 'Can you hear it'?
- 'Rinne test' and 'Weber test' may be necessary (normally, air conduction is better than bone conduction).

IXth and Xth Cranial Nerves

- While talking with the patient, observe any nasal voice or hoarseness (hoarseness indicates bilateral paralysis of superior laryngeal branch of vagus). If it is unilateral, then it is usually asymptomatic.
- Ask the patient about any nasal regurgitation.
- 'Open your mouth and say aah': See palatal movement (arching of palate). If one side remains flat and immobile, it indicates paralysis of that side (soft palate is pulled to the normal side).
- Ask to cough: If bovine cough, indicates recurrent laryngeal nerve palsy.
- Palatal reflex (gag reflex, IXth nerve): Touch back of pharynx and see constriction.
- Taste sensation in posterior one-third of tongue (IXth nerve).

XIth Cranial Nerve

Ask the patient, 'Shrug your shoulder against resistance' (trapezius muscle).

'Turn your head to the other side against resistance; feel sternocleidomastoid' (test on both sides).

XIIth Cranial Nerve

Look at the tongue to see any:

- Wasting.
- Fasciculation.
- Small and spastic or tight.

Ask the patient: 'Put out your tongue' . Observe the following:

- If small and spastic (unable to protrude).
- Deviation (towards the weak side).

Ask the patient, 'Waggle your tongue' . Feel the weak side.

N.B. Remember the following points:

- In unilateral UMN lesion, there may not be any change in tongue.
- In bilateral UMN lesion, tongue is small, spastic and unable to protrude (found in pseudobulbar palsy, IXth, Xth and XIIth cranial nerve palsy.)
- In LMN type of lesion, there is wasting, fasciculation and weakness of tongue (found in bulbar palsy, IXth, Xth and XIIth cranial nerve palsy.)

Facial (VIIth) Nerve Palsy

Usual instructions are:

- Look at the face. What are your findings? What else do you want to examine?
- Examine the face.
- Examine the facial nerve.

Presentation of Case No. 1 (Instruction 1—by Looking Face, Suppose Left)

- Facial asymmetry.
- Drooping of the left corner of mouth.
- Left eye appears wide and open.
- Nasolabial fold: Less pronounced.

Q: What else do you want to examine?
A: I want to examine VIIth cranial nerve.

Presentation of Case No. 2 (Instruction 2 or 3—Suppose Left Side)

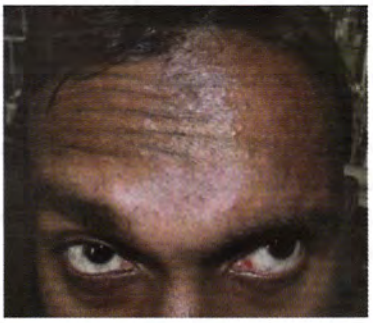
- There is failure of wrinkling of forehead of left side.
- The left eye cannot be closed; and on attempting to close, there is Bell phenomenon (eyeball is rolled upwards and outwards).
- There is weakness of left side of face on puffing the cheek.
- Failure to whistle and smile.
- While showing the teeth, lips are drawn to right side.

My diagnosis is **left-sided Bell palsy.**

Q: Why it is Bell palsy?
A: Because Bell phenomenon is present along with facial palsy.



Left-sided Bell palsy (Bell phenomenon)



Failure of wrinkling of forehead (left)



Left eye—wide and open



Showing teeth—lips drawn to right



Failure to whistle

Q: Why it is called Bell palsy?
A: Due to the presence of Bell phenomenon.

Q: What **else** do you want to examine?
A: As follows:

- Taste sensation in anterior two-thirds of the tongue (chorda tympani).
- Palate and external auditory meatus to see any vesicle (Ramsay Hunt syndrome).
- Evidence of hyperacusis.

Q: What is **Bell palsy?**
A: It is an LMN type of facial palsy.

Q: What are the **causes** of Bell palsy?
A: Idiopathic in 95% cases; it may be related to viral infection due to reactivation of latent herpes simplex virus I.

Q: Where is the **site of lesion** in Bell palsy?
A: Facial canal, in petrous part of temporal bone (in stylomastoid foramen).

Q: What is **Bell phenomenon?**
A: On attempting to close the eyes, the eyeball rolls upwards and outwards, and is called Bell phenomenon. It is a normal phenomenon, but cannot be seen because eyes are closed. It is only seen in Bell palsy.

Q: What is the **relation** between diabetes mellitus and Bell palsy?
A: Diabetes mellitus is thought to be responsible for 10% of the cases of Bell palsy.

Q: What are **muscles tested** in Bell palsy?
A: As follows:

- Frontal belly of occipitofrontalis (wrinkling of forehead).
- Orbicularis oculi (closer of eyes).
- Corrugator supercilii (frown).
- Buccinator (puffing of cheek).
- Orbicularis oris (whistling).
- Levator anguli oris and risorius (showing the teeth and smiling).
- Stapedius muscle (hyperacusis).

Q: How to **treat** Bell palsy?
A: As follows:

- Prednisolone 40–60 mg daily for 1 week should be given within 72 h.
- In severe case, prednisolon **plus** antiviral (acyclovir or valaciclovir) may be given within 72 h.
- Physiotherapy: Facial exercise and electrostimulation within 14 days.
- Protection of eye during sleep (shut with tape, or even tarsorrhaphy), artificial tears or ointment.
- Residual paralysis may occur in 10% cases. Cosmetic surgery may be helpful.

During recovery, aberrant reinnervation may occur producing unwanted facial movement and tear during salivation (called **crocodile tear).**

Q: What is the **prognosis** of Bell palsy?
A: As follows:

- Spontaneous improvement begins in 2nd week, 70–80% cure within 12 weeks. May take 12 months. Less than 10% may have residual weakness.
- Prognosis can be detected by EMG: Reduction of amplitude of facial muscle action potential in the 1st week indicates slow or incomplete recovery.

Q: What is **Ramsay Hunt** syndrome? How to **treat?**
A: It is the herpes zoster of geniculate ganglia characterized by:

- Ipsilateral VIIth cranial nerve palsy (lower motor neuron).
- Rash (herpetic vesicles) in the external auditory meatus and soft palate.
- Ipsilateral loss of taste and buccal ulceration.
- Deafness and Vth nerve lesion may also occur.

Treatment: Antiviral like famciclovir may be given. However, complete recovery is less likely than Bell palsy.



Bilateral Bell palsy (Bell phenomenon in both eyes)



Bilateral facial weakness in myasthaenia gravis

Causes of bilateral facial palsy

- Guillain–Barré syndrome (GBS).
- Sarcoidosis.
- Bilateral Bell palsy (rare).
- Bilateral parotid disease.
- Lyme disease.
- Any cause of mononeuritis multiplex (rare).

Causes of bilateral facial weakness

- Bilateral facial palsy.
- Myasthaenia gravis.
- Myopathy (fascio–scapulo–humeral myopathy and myotonic dystrophy).

N.B. Myasthaenia gravis and some myopathy may mimic bilateral facial palsy. However, these are not due to nerve involvement.

Presentation of a Case (LMN Type of Facial Palsy): Case No. 3

- Just like Case 1, but there is no Bell phenomenon.

My diagnosis is **LMN type of facial palsy.**

Q: Why LMN type of facial palsy?

A: Because both upper and lower parts of face are affected.

Q: Why not **UMN type** of facial palsy?

A: In UMN of facial palsy, only lower part of face is involved, as muscles of upper part of face are bilaterally innervated.

Q: How to locate the **site of lesion** in LMN facial palsy and what are the **causes**?

1. Lesion in pons:
 - Associated VIth nerve palsy (lateral rectus muscle of eye) and Vth nerve palsy.
 - If corticospinal tract is involved, there is contralateral hemiplegia. (Causes—vascular, demyelinating disease, tumour and syringobulbia.)
2. Cerebellopontine angle lesion:
 - Usually associated with Vth, VIth and VIIth nerve palsy and also cerebellar signs. (Causes—acoustic neuroma, neurofibroma and meningioma.)
3. Lesion in petrous part of temporal bone:
 - Associated with loss of taste in anterior two-thirds of the tongue and also hyperacusis. [Causes—Bell palsy, Ramsay Hunt syndrome, trauma and chronic suppurative otitis media (CSOM)].
4. Lesion in face:
 - Parotid tumour, sarcoidosis, and trauma or surgery of parotid gland.

Presentation of a Case (UMN Type—Supposing on Right Side): Case No. 4

- Asymmetry of face on the right side. Wrinkling of forehead is normal on both sides.
- The patient can close the eyes properly (upper part of face is not involved).
- There is involvement of lower part of the face (as evidenced by impaired puffing of the cheek, smiling, whistling and showing the teeth).

My diagnosis is **right-sided UMN type of facial palsy.**

Q: Why **UMN lesion**? What **else** do you want to see and Why?

A: It is UMN lesion because only the lower part of face is affected and upper part is spared. I want to see if the patient has hemiplegia (ask the patient to raise the arms and legs) because common cause of UMN facial palsy is CVA, involving internal capsule, which is associated with hemiplegia.

Q: Is there any **isolated UMN facial palsy** without hemiplegia?

A: Yes, if the lesion occurs in the contralateral frontal complex (involving inferior frontal branch of the middle cerebral artery).

Q: What are the **differences** between UMN and LMN type of facial palsy?

A: As follows:

Topic	UMN	LMN
Site of lesion	Above the facial nucleus, commonly in internal capsule	In the facial nucleus and distal to the nucleus
Involved area	Lower part of face	Both upper and lower part of face
Bell phenomenon	Absent	May be present
Taste sensation	Not affected	May be affected

Hyperacusis	Absent	May may occur, if nerve to the stapedius is involved
Facial wasting or atrophy	Absent	May be present
Associated feature	Usually associated with hemiplegia	Not so (contralateral hemiplegia, if pontine lesion); other findings according to site of lesion

VIth Nerve Palsy

Usual instructions are:

- Examine the eyes or look at the eyes. What else do you want to examine?
- See the movement of eyes.

Presentation of a Case (supposing right sided)

- The patient has convergence squint in right eye at rest.
- There is no lateral movement of right eye; and on attempting to look on that side, there is diplopia (outermost image comes from the affected eye).
- Now test for diplopia with covering the eye; the outer image disappears on covering the affected eye.

My diagnosis is **right-sided VIth nerve palsy.**

Q: What does **diplopia** look like in VIth nerve palsy?

A: Image looks parallel and horizontal to each other (if the image is oblique or angular, it indicates superior oblique palsy).

Q: What are the **causes of VIth nerve palsy?**

A: As follows:

- Raised intracranial pressure is the commonest cause, due to stretching of the nerve in its long intracranial course (a false localising sign).
- Brainstem lesion (vascular, neoplastic and MS).
- Cavernous sinus lesion (tumour, thrombosis, infection, aneurysm).
- Trauma.
- Any cause of mononeuritis multiplex.
- Idiopathic (common).
- Subacute meningitis (due to fungal, tuberculous, lymphomatous, carcinomatous).
- Diabetes mellitus.
- Others: Sarcoidosis, giant cell arteritis, Lyme disease, acoustic neuroma and nasopharyngeal carcinoma.

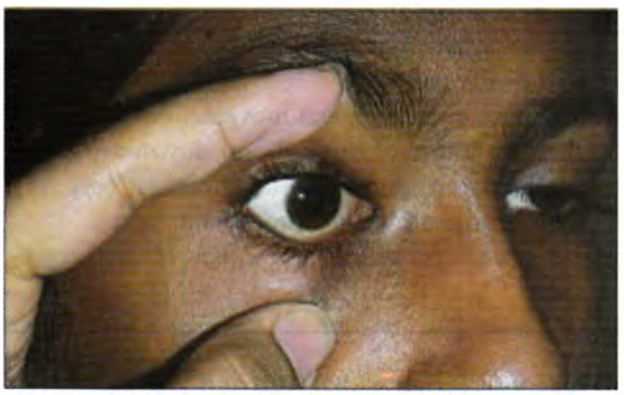
Q: What are the **causes of bilateral VIth nerve palsy?**

A: As follows:

- Trauma.
- Wernicke encephalopathy.
- Mononeuritis multiplex.
- Raised intracranial pressure (VIth nerve palsy is often associated with VIIth nerve lesion also).



Right-sided VIth nerve palsy



Right-sided VIth nerve palsy—failure of abduction

Multiple Cranial Nerve Palsy

Presentation of a Case (Supposing IIIrd, IVth and VIth Nerve Palsy): Case No. 1

- There is ptosis.
- No movement of eyeball in any direction.
- On attempting to look at the right or left, there is diplopia.
- Pupil is dilated, no reaction to light, both direct and consensual.

My diagnosis is **IIIrd, IVth and VIth nerve palsy.**

Q: What are the causes?

A: As follows:

1. Raised intracranial pressure due to any cause:
 - Meningitis.
 - Encephalitis.
 - Sarcoidosis.
 - Neoplasm.
 - GBS.
2. Brainstem lesion:
 - Vascular (CVA).
 - Neurosyphilis.
 - MS.
 - Syringobulbia.
3. Mononeuritis multiplex (due to any cause).
4. Cavernous sinus thrombosis or carotid-cavernous fistula.



Left-sided ptosis due to IIIrd nerve palsy



Left eye—failure of adduction and dilated pupil (IIIrd nerve palsy)

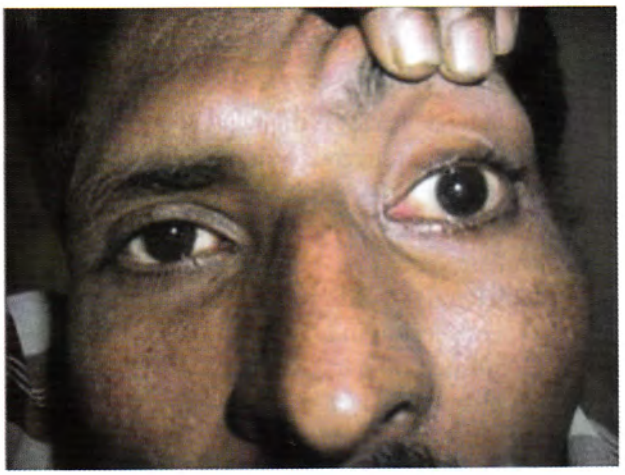
Presentation of a Case (IIIrd and VIth Nerve Lesion—Supposing Right Side): Case No. 2

- There is ptosis on right side.
- Pupil is dilated; no reaction to light (both direct and consensual).
- There is failure of lateral movement of eye; also there is failure of upward and downward (eye in abduction) and upward movement (eye on adduction), and medial movement.
- Diplopia is present on movement of the lateral gaze.

My diagnosis is **right-sided IIIrd and VIth cranial nerve lesion.**



Left-sided ptosis and failure of wrinkling due to facial palsy



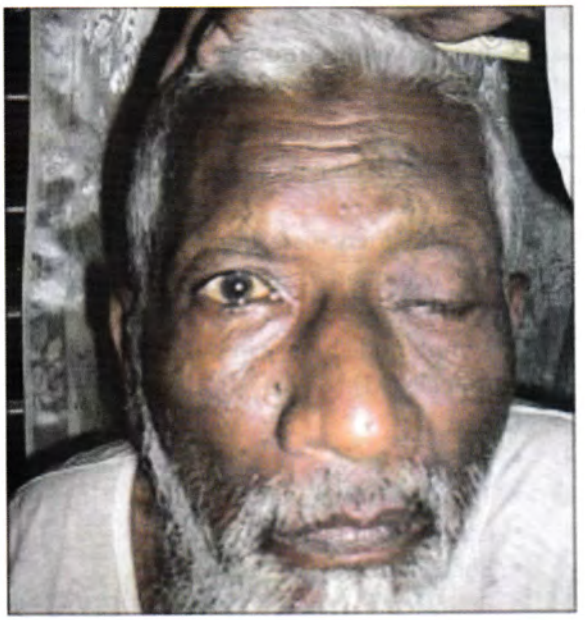
Failure of abduction (left) due to VIth nerve palsy



Failure of elevation and depression of eyeball (inferior and superior oblique palsy—eyeball medially)



Failure of elevation and depression of eyeball (superior and inferior rectus palsy—eyeball laterally)



Left IIIrd nerve palsy and right VIIth nerve palsy

Q: What are the causes?

A: As follows:

- Raised intracranial pressure due to any cause.
- Mononeuritis multiplex.
- Meningitis.
- Encephalitis.
- Trauma.

Presentation of a Case (IXth, Xth and XIIth Cranial Nerve Palsy): Case No. 3

- There is hoarseness of voice, nasal regurgitation and nasal voice.
- Palate movement is absenst.
- Gag reflex is absent.
- Tongue is spastic, wasted and weak. There is fasciculation in the tongue.

My diagnosis is **IXth, Xth** and **XIIth cranial nerve palsy.**

Q: What are the causes of IX, X, XI and XIIth cranial nerve palsy?

A: According to the site of lesion:

1. Within brainstem:
 - Infarction.
 - Syringobulbia.
 - MND.
 - Poliomyelitis.
2. Around skull base:
 - Carcinoma of nasopharynx.
 - Glomus tumour.

- Neurofibroma.
- Jugular venous thrombosis.
- Trauma.

3. Within neck and nasopharynx:
 - Carcinoma of nasopharynx.
 - Metastases.
 - Carotid artery dissection (XII).
 - Polyneuropathy.
 - Trauma.
 - Lymph node biopsy in posterior triangle (XI).
4. Others:
 - GBS.
 - Tubercular meningitis.
 - Carcinomatous meningitis.
 - Encephalitis.
 - Brainstem lesion, vascular (CVA) and neoplastic.
 - Bulbar and pseudobulbar palsy.
 - Neurosyphilis.
 - Mononeuritis multiplex.

Remember the site of lesion involving multiple cranial nerves

- Unilateral IIIrd, IVth, Vth and VIth nerve involvement suggests lesion in cavernous sinus.
- Unilateral Vth, VIIth and VIIIth nerve involvement suggests lesion in cerebellopontine angle.
- Unilateral IXth, Xth and XIth nerve involvement suggests lesion in jugular foramen.
- Combined bilateral Xth, XIth and XIIth nerve involvement suggests bulbar palsy, if LMN lesion signs are present; and pseudobulbar palsy, if UMN lesion signs are present.

Actions of extraocular muscles:

- When eye is abducted, elevator is superior rectus and depressor is inferior rectus (both supplied by IIIrd nerve).
- When eye is adducted, elevator is inferior oblique (supplied by IIIrd nerve) and depressor is superior oblique (supplied by IVth nerve).

CVD with Hemiplegia

Usual instructions are:

- Examine the lower limb or examine the upper limb.
- Perform the neurological examination of upper or lower limbs.

Presentation of a Case

- There is difficulty in raising the right leg and right arm.
- Muscle tone is increased in both right upper and lower limbs, but normal in left limbs.
- Motor power is diminished; grade 0/5 in right upper and lower limbs, but normal in left side.
- Deep tendon reflexes are exaggerated in right limbs and normal in left limbs.
- There is ankle clonus on the right side.
- Plantar response is extensor on the right side and flexor on the left side.
- Sensory functions – normal.
- There is a urinary catheter in situ.

My diagnosis is **right-sided hemiplegia more likely with CVD**.

Q: What **else** do you want to examine?
A: I want to examine the speech and cranial nerves. Also, I want to examine the blood pressure, the heart and the neck (bruit) to find out the cause.

Q: What would you look for in the **heart?**
A: Any arrhythmia like atrial fibrillation and any valvular lesion.

Q: What would you look for in the **neck?**
A: Carotid bruit (thrombus from carotid may be dislodged and cause cerebral thrombosis).

Q: What is the **cause** of CVD in this patient?
A: I would like to take the history of hypertension, any cardiac problem and also the onset, history of unconsciousness, headache, etc. The causes may be:

- Cerebral infarction: Commonest cause.
- Cerebral haemorrhage.

Q: What is the likely **site of lesion** in your case?
A: Left internal capsule due to involvement of lenticulostriate branch of middle cerebral artery.

Q: What are the **diseases** included in **CVA?**
A: As follows:

- Cerebral haemorrhage.
- Cerebral thrombosis.
- Cerebral embolism.
- Subarachnoid haemorrhage.
- Hypertensive encephalopathy.
- Cerebellar haemorrhage.
- Cerebellar infarction.

Q: What **investigations** do you suggest?

A: As follows:

1. CT scan of the head (first investigation to be done).
2. Complete blood count with ESR.
3. Blood sugar.
4. Blood urea and serum creatinine.
5. Fasting lipid profile.
6. Serum electrolytes.
7. Chest X-ray PA view.
8. ECG.
9. Source of the event:
 - Doppler study of extra-/intracranial vessels.
 - Echocardiography: Transthoracic or transoesophageal.
 - MRA or CTA of the cerebral vessels.
 - DSA of the cerebral vessels (gold standard to find out AVM or aneurysm).

Q: What is **stroke**? What are the **types** of stroke?

A: Stroke may be defined as sudden development of focal neurological deficit due to nontraumatic vascular cause, lasting for more than 24 h. It is of following subvarieties:

- Transient ischaemic attack (TIA): Sudden neurological dysfunction due to cerebral ischaemia lasting less than 24 h; and the patient recovers completely within 24 h.
- Stroke in evolution: The symptoms worsen gradually or in a step-wise pattern over hours or days, and the neurological deficit persists for more than 24 h.
- Completed stroke: Clinical signs of neurological deficit are persistent.
- Reversible ischaemic neurological deficit (RIND): Neurological deficit persists for more than 24 h, but recovers completely within 3 weeks.
- Partial nonprogressive stroke (PNS): Neurological deficit persists for more than 3 weeks, but is either partial or ends up with minimal residual deficit.

Q: What are the **features of CVD** according to the site of involvement of different parts of brain?

A: As follows:

1. Cortical:
 - Usually monoplegia.
 - If lesion is extensive, contralateral hemiplegia may occur.
 - Speech disturbance may be present, if the lesion involves the dominant hemisphere.
 - Jacksonian convulsions and headache may occur.
 - There may be cortical type of sensory loss, e.g. astereognosis.
2. Subcortical:
 - Usually monoplegia.
 - May be contralateral hemiplegia.
 - Speech disturbance may be present.
 - There may be loss of postural sensibility, tactile localization and discrimination of the affected limbs due to involvement of thalamocortical fibres.
3. Internal capsule:
 - Contralateral hemiplegia.
 - Hemianaesthesia due to damage of the sensory fibres and homonymous hemianopia due to damage of visual fibres—both of which lie posterior to the pyramidal tract in internal capsule.
 - Global aphasia in left-sided lesion.
 - VIIth cranial nerve palsy on the side of palsy—UMN type.
4. Brainstem:
 - Symptoms are: Vertigo, nausea, vomiting.
 - Crossed hemiplegia, brainstem syndrome, pupillary abnormality, cerebellar involvement, gaze paralysis, Horner syndrome.
 - If pons is involved: There is deep coma, pin-point pupil, hyperpyrexia, decerebrate or decortical rigidity, absence of lateral eye movement on head turning.
 - If involvement of midbrain and medulla: There is loss of consciousness, quadriplegia, Cheyne–Stokes breathing, decerebrate rigidity.

Q: How to **treat** CVD?

A: As follows:

1. General measures:
 - Nasogastric tube feeding.
 - Regular change of posture (2 hourly).
 - Care of bowel, bladder (catheterization), mouth (to prevent fungal infection), and eyes (tear naturale or taping of the affected eye shut).
2. Control of risk factors: Hypertension, diabetes mellitus, hyperlipidaemia, etc.
3. If cerebral oedema: Dexamethasone or mannitol.
4. Specific treatment according to the type of stroke (after CT scan):
 - Cerebral infarction: Antiplatelet drugs (e.g. aspirin, clopidogrel). Cerebral vasodilator like vinpocetin should be given. If atrial fibrillation, heparin followed by warfarin should be considered.
 - Cerebral haemorrhage: For massive haemorrhage, neurosurgical intervention

may be required. Other treatment is symptomatic and supportive.
- Subarachnoid haemorrhage: Nimodipine can be given, whereas neurosurgical intervention is essential.

5. To reduce morbidity and improve quality of life: Physiotherapy, speech therapy, occupational therapy, etc.

Q: What is the **prognosis** of CVA?

A: Prognosis depends on the type of lesion, site, extent of involvement and associated primary risk factors.
- Mortality rate is higher in intracerebral haemorrhage than embolic stroke.
- In cerebral infarction, immediate prognosis is better, long-term prognosis depends upon extent of damage.
- In cerebral haemorrhage, immediate prognosis is worse.
- In haemorrhagic stroke, 25% die within first 2 years, 10% die within first month. However, prognosis is better in the long run, when the haematoma resolves.
- One-third returns to independent mobility; one-third becomes disabled.

Q: What are the causes of **recurrent hemiplegia**?

A: As follows:

1. CVD due to:
 - Atrial fibrillation.
 - Hyperviscosity syndrome.
 - Homocystinuria.
 - Amyloidosis.
 - Deficiency of protein C, S or antithrombin III.
 - Polycythaemia rubra vera.
 - Antiphospholipid syndrome.
 - Polyarteritis nodosa.
 - Wegener granulomatosis.
 - Takayasu arteritis.
2. Other causes:
 - MS.
 - Hemiplegic migraine.
 - Epilepsy (Todd palsy).
 - Hysteric hemiplegia.

Q: What are the causes of CVD in a **young patient**?

A: As follows:
- Mitral stenosis with atrial fibrillation (cerebral embolism from cardiac source).
- Other cardiac cause: PFO, VSD, TOF.
- Antiphospholipid syndrome.
- SLE.
- Haematological disease: Sickle cell anaemia, polycythaemia rubra vera, inherited deficiency of naturally occurring anticoagulant (protein C, protein S, antithrombin III, factor V Leiden). In all these conditions, there is increased tendency of thrombosis.
- Vasculitis, Behcet disease.
- Vascular malformation: AVM, berry aneurysm causing SAH.
- Dissecting aneurysm.
- In female: Oral contraceptive pill, eclampsia.
- Homocystinuria.
- Syphilis.
- Premature atherosclerosis may occur in familial hyperlipidaemia.
- Rarely, migraine may cause cerebral infarction.
- Drugs like amphetamine, cocaine.

Q: What **investigations** should be done in a young patient with stroke?

A: See as above. For young patient, specific investigations are as follows:
- Chest X-ray, ECG and echocardiography (to exclude cardiac problem like MS with AF, other cardiac problem like PFO, TOF).
- CBC, ESR: It will also exclude polycythaemia rubra vera.
- Serum lipid profile: To exclude juvenile hyperlipidaemia.
- For collagen vascular disease: ANA, anti-dsDNA, anticardiolipin and antiphospholipid antibody.
- Perinuclear antineutrophil cytoplasmic antibody (P-ANCA), cytoplasmic antineutrophil cytoplasmic antibody (C-ANCA).
- Coagulation screening, serum antithrombin III, protein C and protein S level.
- Others: Red cell mass (PRV), chromatographic test in serum and urinary level of homocystine or methionine (homocystinuria), TPHA and VDRL (syphilis).

Q: What are the **risk factors** for stroke?

A: Risk factors are variable for ischaemic stroke and haemorrhagic stroke:

Risk factors for **ischaemic** stroke:
- Nonmodifiable:
 - Age.
 - Gender.
 - Ethnicity or race.
 - Genetics.
 - Family history.
- Modifiable:
 - Hypertension.
 - Smoking.
 - Lifestyle.

- Diabetes mellitus.
- Obesity.
- Heart disease (atrial fibrillation, ischaemic heart disease, cardiomyopathy, etc.).
- Dyslipidaemia.
- Oral contraceptive pill.
- Alcohol.
- Previous history of stroke or TIA.
- Carotid vessel atherosclerosis.
- Atheromatous aortic arch.
- Diseases like homocystinuria, hyperfibrinogenaemia, deficiency of protein C, S and antithrombin III, polycythaemia rubra vera, antiphospholipid syndrome, thrombotic thrombocytopenic purpura, sickle cell anaemia, protein V Leiden syndrome, vasculitis (like polyarteritis nodosa, Wegener granulomatosis, Takayasu arteritis), migraine.
- Abuse of cocaine, use of COX-2 inhibitor (slightly increased incidence of stroke).

Risk factors for **haemorrhagic** stroke:

- Hypertension.
- AVM.
- Aneurysm.
- Amyloid angiopathy.
- Cavernous angioma.
- Anticoagulant therapy.
- Hypercoagulable disorder.
- Drugs: Cocaine, amphetamine.
- Vasculitis: SLE, polyarteritis nodosa (PAN), isolated CNS vasculitis.
- Septicaemia.
- Moyamoya disease.
- Haemorrhage into brain tumour.

Q: How to **prevent** stroke?

A: As follows:

- Risk factors like hypertension, diabetes mellitus, obesity, etc. should be identified and controlled.
- Smoking and alcohol should be stopped.
- Antiplatelet drug, e.g. aspirin.
- Life style modification: Regular physical exercise, dietary modification.
- Statin should be given to all patients.
- If there is atrial fibrillation: Treatment of primary cause and anticoagulation.
- Treatment of primary cause.

Brainstem syndrome

1. Weber syndrome: Ipsilateral paralysis of IIIrd cranial nerve (LMN type) with contralateral hemiplegia (crossed hemiplegia). Paralysis of upward gaze is usually present. Lesion is at midbrain.
2. Millard–Gubler syndrome: Paralysis of VIth cranial nerve (LMN type) with or without VIIth cranial nerve palsy (LMN type) with contralateral hemiplegia (crossed hemiplegia). Lesion is at pons.
3. Lateral medullary syndrome (posterior inferior cerebellar artery thrombosis, also called Wallenberg syndrome): The patient presents with acute vertigo, nausea, vomiting and diplopia, cerebellar and other signs. Features depend on the precise structures damaged and may include:
 - Ipsilateral:
 i. Trigeminal: Diminished pain and temperature (due to the involvement of descending tract and nucleus of trigeminal nerve).
 ii. Cerebellar sign (due to the involvement of cerebellum and its connection).
 iii. Horner syndrome (due to the involvement of descending sympathetic tract).
 iv. Palatal paralysis and diminished gag reflex (there may be hoarseness and dysphagia due to vocal cord paralysis because of IXth and Xth nerve lesion).
 v. Diplopia (VIth nerve involvement).
 - Contralateral:
 i. Loss of pain and temperature due to spinothalamic tract involvement (in the trunk, limbs, may be in face). It is called dissociated sensory loss.
 - When there is isolated occlusion of PICA, pyramidal pathways escape and there is no hemiplegia. However, in majority of the cases, there is vertebral artery involvement and pyramidal signs (hemiplegia) are present.
4. Medial medullary syndrome:
 - It is due to occlusion of lower basilar artery or vertebral artery or one of its medial branches. It is characterized by contralateral hemiplegia, which spares the face, contralateral loss of vibration, and joint position sense, ipsilateral paralysis and wasting of tongue.

N.B. Remember the following points:

- Damage to brainstem reticular activating system leads to coma.
- Upper brainstem infarction (ventral pons) leads to the locked-in syndrome.
- Pseudobulbar palsy may occur after lower brainstem infarction (medullary infarction, bilateral cerebral infarction).

Q: What are the **causes of coma** or unconsciousness?

A: As follows (remember the mnemonic **AEIOU–DAMH**):

- **A**poplexy: Cerebral haemorrhage, subarachnoid haemorrhage, etc.
- **E**pilepsy.
- **I**nfection (e.g. encephalitis, meningitis, cerebral malaria, severe septicaemia).
- **O**pium poisoning.
- **U**raemia (renal failure).
- **D**iabetes mellitus [ketoacidosis, hypoglycaemia, lactic acidosis, hyperosmolar non-ketotic diabetic coma (hyperglycaemic hyperosmolar state), drug poisoning (sedative)].
- **A**lcohol.
- **M**etabolic: Metabolic acidosis.
- **H**ypoglycaemia, hypoxaemia, hypertensive encephalopathy, hepatic coma, hypothyroidism (myxoedema coma), hyponatraemia, hypothermia, hyperpyrexia, head injury.

Gait Abnormality

Usual instruction:

- Look at the gait. What is your diagnosis?

Presentation of a Case

- The patient has broad-based reeling or drunken gait.

My diagnosis is **cerebellar gait**.

Q: What **else** do you like to see?

A: I would like to see other signs of cerebellar lesion, such as:

- Titubation.
- Tilting towards the site of lesion.
- Nystagmus (horizontal).
- Scanning speech.
- Intention tremor.
- Incoordination.
- Dysdiadochokinesis.
- Past-pointing (dysmetria).
- Ataxia.
- Hypotonia.
- Diminished tendon reflex (knee jerk may be pendular).

Q: What are the **causes** of cerebellar lesion?

A: See in 'cerebellar lesion'.

Q: What are **different types** of gait?

A: As follows:

- Cerebellar gait: Broad-based reeling or drunken gait. It is found in cerebellar lesion.
- Parkinsonian gait: Festinate gait mainly (for details, see in 'Parkinsonism').
- Stamping gait: The patient raises the foot suddenly and tends to throw forward, bringing it to the ground with a stamp, often heel first. It is found in sensory ataxia.
- High stepping gait: The patient lifts his foot high to avoid scrapping the toes. It is found in foot drop.
- Hemiplegic gait: The patient has difficulty in bending the knee and drags the hemiplegic limb in a semicircle-like motion with the toes scrapping the floor and the forefoot flops to the ground before the heel. This is found in hemiplegia.
- Scissor gait: During walking, one leg crosses in front of the other. It is found in spastic paraplegia, usually due to cerebral palsy.
- Waddling gait: The patient walks on a wide base with trunk moving side-to-side and pelvis drooping on each side. At each step toes touch the ground before the heel. It is found mostly in myopathy, osteodystrophy, bilateral hip joint disease, etc. There is increased lumbar lordosis.
- Marche a petits pas: There is slow movement. The patient walks with very short, shuffling and irregular steps with loss of associated movements. The gait is similar to that of Parkinson disease. It is seen in normal pressure hydrocephalus.

Q: What is **astasia abasia**?

A: This is seen in patient with psychogenic disturbance. The patient is unable to walk, to stand, falls far to the side on walking but usually regains balance before hitting the ground. The legs may be thrown out widely or the patient may kneel with each step.

Orofacial Dyskinesia

Usual instruction:

- Look at the face. Or look at the patient.

Presentation of a Case

- There is orofacial dyskinesia with chewing, pouting, lip smacking, grimacing and tongue movement.
- There is choreoathetosis of the limbs and trunk.

My diagnosis is **Orofacial dyskinesia**.

Q: What **history** do you like to take?

A: I would like to take drug history. Usually, there is history of prolonged intake of neuroleptic drugs.

Q: If there is history of intake of **neuroleptic** drugs, what will be the diagnosis?

A: Tardive dyskinesia. Tardive means after chronic exposure to dopamine receptor blockers (such as antipsychotic, antiemetic).

Q: What is **tardive dyskinesia**?

A: Tardive dyskinesia (TD) is a drug-induced disorder characterized by orofacial dyskinesia such as lip smacking, chewing, pouting, grimacing, rhythmic tongue movement and choreoathetoid movement.

Involuntary movements involve the tongue, lips, face, trunk and extremities that have persisted for at least 4 weeks and that began during treatment with neuroleptics or within 4 weeks of discontinuing neuroleptics.

Diagnosis of neuroleptic-induced TD generally requires history of taking neuroleptics for at least 3 months. It may persist or even get worse after the withdrawal of drug.

TD is most common in patients with schizophrenia, schizoaffective disorder or bipolar disorder who have been treated with antipsychotic medication for long periods; but occasionally occur in other patients as well.

TD is due to altered dopamine receptor sensitivity induced by the drug.

Q: What are the drugs that may **cause** tardive dyskinesia?

A: It is usually due to use of neuroleptics like phenothiazines (e.g. chlorpromazine) and butyrophenones (e.g. haloperidol) for at least 6 months. Other drugs include:

- Antiemetic: Metoclopramide (D2 dopamine receptor antagonist).
- Antiepileptic: Phenytoin, carbamazepine, phenobarbital, ethosuximide.
- Others: Reserpine, tetrabenazine, antihistamines, fluoxetine, amoxapine.

N.B. Quetiapine and olanzapine causes less TD.

Q: What **other extrapyramidal complications** may occur due to neuroleptics?

A: As follows:

- Acute dystonia: Occurs soon after starting the drug. Usually due to metoclopramide, prochlorperazine. This is treated by IV benzatropine or procyclidine. Also, the offending drug should be stopped.
- Akathisia (uncontrollable restlessness, repetitive and irresistible need to move).
- Parkinson syndrome.

Q: How to **treat** TD?

A: The drug should be stopped. Tetrabenazine may help.

Q: What are the **different types** of dyskinesias?

A: As follows:

- Chorea.
- Athetosis.
- Tic.
- Tortion dystonia.
- Hemiballismus.

Foot Drop

Usual instruction:

- Examine the lower limb of the patient.

Presentation of a Case

- There is wasting of anterior tibial and peroneal group of muscles on the right lower limb.
- Dorsiflexion and eversion of right foot is weak.
- Ankle jerk is normal.
- Sensation over the lateral aspect of right leg and dorsum of right foot is impaired.

My diagnosis is **right-sided foot drop**.



Foot drop (right)

Q: Where is the **lesion**?

A: Common peroneal (lateral popliteal) nerve palsy.

Q: What are the branches of common peroneal nerve?

A: There are two branches:

- Superficial peroneal nerve: Sensory to lateral calf and dorsum of foot; also responsible for eversion of foot (motor).
- Deep peroneal nerve: Dorsiflexion of foot and toe, sensation to the web space between first and second toes.

Q: **Can it** be due to deep peroneal nerve palsy?

A: In deep peroneal nerve palsy, the sensory deficit will be limited to the area between the first and second toes.

Q: What are the **reflex and planter responses** in common peroneal nerve palsy?

A: Both normal.

Q: What **else** do you like to examine? What **findings** do you expect?

A: I want to examine the gait. There will be high-stepping gait (the patient lifts his foot high to avoid scrapping the toes, and there is an audible 'clop' of the foot as he walks). Also, the patient will be unable to stand on the right heel.

Q: What is the **site** of the lesion of common peroneal nerve palsy?

A: The nerve is usually injured at the head of the fibula due to fracture or compression by a tourniquet or splints.

Q: What are the **causes** of common peroneal nerve palsy?

A: As follows:

- Trauma (to the nerve, fibular fracture, total knee arthroplasty or proximal tibial osteotomy).
- Compression by plaster or tourniquet around the knee, ganglion arising from superior tibiofibular joint.
- Leprosy.
- Old polio.
- Any cause of mononeuritis multiplex: diabetes mellitus, polyarteritis nodosa, collagen vascular disease, etc.

Q: What **investigation** should be done to diagnose common peroneal nerve palsy?

A: Nerve conduction study (local conduction block or slowing in the region of the head of the fibula).

Q: How to **treat** common peroneal nerve palsy?

A: As follows:

- Surgery, if the nerve is severed.
- Use of splint and calliper shoes for intact and concussed nerve.

Q: What are the **causes** of foot drop?

A: As follows:

- Peripheral neuropathy.
- Common peroneal nerve palsy.
- Sciatic nerve palsy.
- Motor neuron disease.
- L4, L5 root lesion.
- Lumbosacral plexus lesion.

Q: What are the **causes** if a patient is unable to walk on heel?

A: As follows:

- Common peroneal nerve palsy
- Charcot–Marie–Tooth disease

Charcot–Marie–Tooth Disease

Usual instruction:

- Examine the lower limb of this patient. Or perform the neurological examination of the lower limb.

Presentation of a Case

- There is wasting of distal muscles of both lower limbs up to the middle of legs, giving rise to inverted champagne-bottle (stork or spindle legs) appearance.
- Bilateral pes cavus and clawing of toes are present.
- Dorsiflexion: Weak in both feet.
- Ankle jerk: Absent bilaterally.
- Plantar response: Bilaterally equivocal or absent.
- Sensory: Mild impairment of both superficial and deep sensation up to mid thigh (even marked sensory loss with trophic ulcer may be found).
- Gait: **High steppage** gait with foot drop.

My diagnosis is **distal motor and sensory neuropathy**, most likely due to **Charcot–Marie–Tooth disease.**

N.B. Always look for scar in the neck of the fibula. If present, it is suggestive of trauma or fracture that may cause common peronial nerve lesion. Palpate the nerve that may be thickened.



Inverted-champagne-bottle appearance of lower limb in Charcot–Marie–Tooth disease

Q: What **else** do you want to see?

A: I want to examine the upper limbs. There may be wasting of small muscles of hands and arm muscles. There may be claw hand.

Q: How does the patient **present**?

A: The patient usually presents with foot deformities or gait disturbance in early childhood or early adult life. Slow progression leads to features of polyneuropathy with distal weakness and wasting that begins in the leg, associated with distal sensory loss, depressed or absent tendon reflexes.

Q: What are the causes of **pes cavus**?

A: It may be unilateral or bilateral.

1. Cause of **bilateral pes cavus**:
 - Charcot–Marie–Tooth disease.
 - Friedreich ataxia.
 - Muscular dystrophies.
 - Spinal muscular atrophy.
 - Cerebral palsy.
 - Syringomyelia.
 - Hereditary spastic paraparesis.
 - Spinal cord tumour.
2. Cause of **unilateral pes cavus**:
 - Old poliomyelitis.
 - Spinal trauma.
 - Spinal cord tumour.
 - Malunion of calcaneus or talus fracture.

Q: What is the **mechanism** of pes cavus in Charcot–Marie–Tooth disease?

A: There is weakness of anterior tibialis and peroneus muscles. The posterior tibialis and peroneus longus antagonize these muscles resulting in pes cavus.

Q: What is the mode of **inheritance**?

A: It is variable, may be autosomal dominant or recessive or X-linked. Affected family members may have forme fruste with only pes cavus and absent ankle jerks.

Q: What are the **types** of peroneal muscular atrophy?

A: As follows:

- Hereditary motor and sensory neuropathy type-I: There is demyelinating neuropathy. It is the commonest type (70%), inherited as autosomal dominant. NCV is reduced.
- Hereditary motor and sensory neuropathy type-II: There is axonal neuropathy. There is prominent sensory involvement with pain and paraesthesia. It is inherited as autosomal dominant (AD) and autosomal recessive (AR). NCV is relatively normal.
- Hereditary motor and sensory neuropathy type-III (also called distal spinal muscular atrophy): There is demyelinating neuropathy. NCV is reduced.
- Other types: CMT with optic atrophy, deafness, retinitis pigmentosa and spastic paraparesis.
- Rarely another type: CMTX—an X-linked dominant hereditary motor sensory neuropathy (HMSN).

Q: What **investigation** do you suggest?

A: Nerve conduction velocity.

- In HMSN type-I: There is marked reduction in motor and sensory conduction velocity.
- In HMSN type-II: Motor conduction velocity is normal or slightly reduced, sensory nerve action potential may be absent, and signs of chronic partial denervation are found in affected muscles electromyographically (EMG).

Q: How to **treat**?

A: No curative treatment, only symptomatic.

- Reassurance and education to the patient.
- Regular exercise and physiotherapy.
- Walking aids.
- Occupational therapy.
- Orthopaedic measures for correction.

Q: What is the **prognosis** of this disease?

A: It is slowly progressive, arrests in middle life. Lifespan is usually normal. Abortive cases are common. Degree of disability is less in spite of marked deformity.

CHAPTER 9

RHEUMATOLOGY

"The rheumatism is a common name for many aches and pains, which have yet got no peculiar appellation, though owing to very different causes"

– William Heberden

Introduction

Rheumatological diseases are commonly selected in any clinical examination. Of these, rheumatoid hand is a very popular short case, though other cases are also common.

Most of the diagnoses are straightforward that can be diagnosed by looking at the patient. It is frequently asked either to examine a particular part of the body or to look at a part for a spot diagnosis. However, even if asked to examine a particular part, "look quickly from head to foot". A good clue for diagnosis may be obvious, such as systemic sclerosis, systemic lupus erythematosus (SLE), dermatomyositis and rheumatoid arthritis (RA). During examination of joints, "always look, feel, move, measure and compare with the other side".

Diseases included are: seropositive and seronegative arthritis, rheumatic fever, fibrositis, neuralgia, myositis, bursitis, gout and other conditions producing somatic pain or soreness and stiffness.



Tophus in gout with chalky discharge



Heberden node in DIP joint and Bouchard node in PIP joint in primary osteoarthrosis

Remember some hallmarks in rheumatological disease:

- Heberden node in distal interphalangeal (DIP) joint and Bouchard node in proximal interphalangeal (PIP) joint are hallmarks of primary osteoarthrosis.
- Rheumatoid nodule is the hallmark of rheumatoid arthritis.
- Tophus is the hallmark of gout.
- Heliotrope rash and Gottron sign are pathognomonic of dermatomyositis.
- Butterfly rash usually indicates SLE.
- Osteophyte (radiologically) is the hallmark of osteoarthrosis.
- Syndesmophyte (radiologically) is the hallmark of ankylosing spondylitis.

Systemic Sclerosis

Usual instructions are:

- Look at the face. What are the findings? What else do you like to examine?
- Examine the hands or legs. What else do you like to examine?

Presentation of a Case (by Looking at the Face): Case No. 1

- The face is smooth, shiny, tight, and immobile with hypopigmented and pigmented areas (salt and pepper appearance).
- Lips are thin, pursed and with puckering.
- Nose is pinched up and tapered (beaking of nose: bird beak face).
- There is loss of wrinkling of forehead and multiple telangiectasia (mention the location).
- Puckering of the skin around mouth, and orifice of mouth is small (microstomia).
- The patient has difficulty in opening the mouth (ask to open the mouth).

My diagnosis is **systemic sclerosis**.



Face in systemic sclerosis

Q: What else do you want to see?

A: I want to examine the hands, legs and skin of other parts of the body (see below).

Presentation of a Case (Hands): Case No. 2

- The skin of both hands is smooth, shiny, tight and thick, and oedematous with pigmented and hypopigmented area.
- Interphalangeal (IP) joints are swollen with flexion contracture.
- There is sclerodactyly (tapering of fingers) and infarction (or ulcer or gangrene) at the tip of finger, and atrophy of pulp is present. May be resorption, beaking of the nails (pseudoclubbing due to resorption), and amputation of finger (may be).
- Telangiectasia at the base of nails.
- There is hard nodule over one finger (calcinosis).

My diagnosis is **systemic sclerosis**.

N.B. If presence of calcinosis, telangiectasia and sclerodactyly, it is called **CREST syndrome** (calcinosis, Raynaud phenomenon, oesophageal involvement, sclerodactyly and telangiectasia) **or CRST syndrome** (calcinosis, Raynaud phenomenon, sclerodactyly and telangiectasia).



Flexion of fingers with skin change (typical hands in systemic sclerosis)



Infarction at the tip of the fingers with flexion contracture

Presentation of a Case (by Looking and Palpating the Skin): Case No. 3

- Skin is pigmented, thick and tight, and also some vitiligo is present.

My diagnosis is **systemic sclerosis**.



Gangrene in left second toe



Infarction of great toe

Q: What is **CREST** or **CRST** syndrome? What questions are asked in CREST syndrome?

A: It is a syndrome characterized by:

- **C:** Calcinosis.
- **R:** Raynaud phenomenon.
- **E:** Esophageal involvement (dysphagia).
- **S:** Sclerodactyly.
- **T:** Telangiectasia.

Ask about Raynaud phenomenon and dysphagia. CREST syndrome is also called limited cutaneous systemic sclerosis, with a better prognosis. Anticentromere antibody is present in serum in 70–80% of the cases (if diffuse deposition of calcium in subcutaneous tissue with presence of acrosclerosis, it is called Thibierge–Weissenbach syndrome).

Q: In systemic sclerosis, what **questions** do you like to ask?

A: The following questions may be asked:

- Do your fingers change colour on exposure to cold? (Raynaud phenomenon).
- If yes, what colours are they? (Pallor, cyanosis and redness.)
- Is there any difficulty in swallowing?
- Is there any difficulty in breathing?
- Is there any bowel abnormality? (Occasional diarrhoea or constipation.)

Q: What is **systemic sclerosis**? What are the **presentations**?

A: It is a connective tissue disease characterized by fibrosis and degenerative changes in skin, vasculature and internal organs. Common in females (F:M = 4:1), age 30–50 years. Usual presentations are:

- Raynaud phenomenon—the commonest 90–97%, may precede by months or years before other symptoms.
- Tightening and thickening of the skin of hands and other parts of the body, arthralgia and arthritis (non-erosive inflammatory), heartburn (reflux oesophagitis due to hiatus hernia), dysphagia, odynophagia, occasional diarrhoea and constipation (blind-loop syndrome) and shortness of breath (DPLD).

Two types of systemic sclerosis are:

- Diffuse cutaneous systemic sclerosis (DCSS): This involves the skin of face and trunk. Also above the knee and elbow (initially, skin is oedematous, thick and tight, and several months later Raynaud phenomenon).
- Limited cutaneous systemic sclerosis (LCSS): This involves skin below the knee and elbow (initially, Raynaud phenomenon, followed by skin change, also called CREST syndrome).

Other varieties (localized):

- Scleroderma sine scleroderma: Involves internal organ without skin lesion.
- Morphoea: Localized, well demarcated, indurated or plaqued, with central hypopigmentation and tethering of skin, usually in extremities and face.
- Linear: If skin involvement is in a linear pattern, usually in lower limbs.

Pathology or pathogenesis in systemic sclerosis:

- Vascular change: Widespread vascular damage in arteries, arterioles and capillaries. There is intimal proliferation, vessel wall inflammation, and endothelial damage with release of cytokines and endothelin-I, the latter causes vasoconstriction. Also, platelet activation.
- Fibrotic change: Fibroblast synthesizes collagen I and III, fibronectin, glycosaminoglycans, producing fibrosis in dermis and internal organs.
- Humoral immunity: Increased during T-lymphocyte and complement activation, autoimmunity and autoantibody production to nuclear antigen.

Q: What are the histological findings of **skin biopsy** in systemic sclerosis?

A: As follows:

- Thinning or absence of epidermis.
- Excess collagen and fibrosis of dermis, loss of appendages in dermis, perivascular infiltration of chronic inflammatory cells (lymphocytes and plasma cells). Blood vessels show intimal proliferation and obliteration.

Q: What **investigations** you would perform in systemic sclerosis?

A: Diagnosis is usually clinical. The following investigations may be done:

1. Complete blood count (ESR is high, but CRP is usually normal unless there is severe organ involvement or coexisting infection).
2. Serology:
 - RA test (positive in 20–30% cases).
 - ANA (positive in 70% cases).
 - Antitopoisomerase 1 or anti-Scl-70 (positive in 30% in diffuse type).
 - Anticentromere antibody (positive 60% in CREST and 10% in diffuse systemic sclerosis) with a speckled nucleolar pattern.
3. Skin biopsy for histopathology.
4. Others:
 - Urine R/E (may be proteinuria).
 - X-ray of the hands (deposition of calcium around the fingers, erosion, resorption of phalanges and disorganization of joints).
 - Chest x-ray (DPLD and honeycomb lung).
 - CT scan of the chest (to detect DPLD).
 - Lung function tests (restrictive lung disease).
 - Barium swallow (dysmotility or reduction of peristalsis, narrowing and dilatation. Hiatus hernia may be present, detected by barium swallow x-ray in Trendelenburg position).
 - Barium follow through.
 - Motility study may be done.
 - Electrocardiogram (ECG).
 - IgG level (raised).

Q: What are the **changes** in the different systems of the body?

A: As follows:

1. Skin changes:
 - In hands and face (see above).
 - Skin in other parts of the body (thick, tight, hyper- or hypopigmented and vitiligo).
 - Skin of the chest is tight and thick (looks like **Roman breast plate**).
2. Joints and muscles: Flexion contracture or deformity. Proximal or distal muscle weakness.
3. Gastrointestinal:
 - Oesophagus: 50% involvement. May be reflux oesophagitis, sliding hiatus hernia, constriction or secondary achalasia, and dysmotility or reduction of peristalsis. Oesophageal manometry shows abnormal and reduced peristalsis in 90%.
 - Stomach: Early satiety, gastric outlet obstruction and recurrent occult upper gastrointestinal tract (GIT) bleeding causing "**watermelon stomach**".
 - Intestine: Hypomotility, bloating, distension, intestinal obstruction or pseudo-obstruction, blind-loop syndrome, diarrhoea and wide-mouth diverticula in colon. Rarely, a serious disorder called **pneumatosis cystoides intestinalis**, in which there is radiolucent cyst or streaks in the wall of small intestine due to air in the intestinal wall (detected by plain x-ray abdomen) can occur. The patient presents with severe abdominal pain.
4. Liver: Primary biliary cirrhosis (PBC) may be associated.
5. Respiratory:
 - DPLD, pulmonary hypertension and cor pulmonale. Pulmonary hypertension may occur without parenchymal lung disease due to pulmonary vessel involvement. Pulmonary hypertension is six times more common in limited type than diffuse type.
 - Others: Pneumonitis, rarely pleural effusion, and alveolar cell carcinoma.
6. Heart: Dysrhythmia, conduction defect, heart failure, cardiomyopathy and pericardial effusion.
7. Kidneys (20% involvement):
 - Renal failure in advanced stage (often fatal).
 - Malignant hypertension (difficult to control, may respond to angiotensin-converting enzyme inhibitors).
8. Endocrine:
 - Hypothyroidism (due to thyroid gland fibrosis).
 - Impotence.
9. Neurologic:
 - Entrapment neuropathy.
 - Facial nerve palsy.
 - Autonomic dysfunction.

Q: How to **manage** systemic sclerosis?

A: There is no specific therapy.

1. General management for Raynaud phenomenon:
 - Exposure to cold should be avoided (by the use of gloves or mittens), lubricants should be used (to avoid dryness).
 - Smoking should be stopped, regular exercise and massage of skin, cleanliness of digital ulcer.
 - Drugs to be avoided (beta-blocker, ergotamine, oral contraceptive and sympathomimetic).
 - Antiplatelet (aspirin) may be given.
 - Calcium antagonist (diltiazem and nifedipine), ACE inhibitor, angiotensin II receptor blocker (valsartan) may be effective.
 - If no response or in severe case, prostacyclin analogue epoprostenol infusion intermittently.
 - If still no response, then surgery (digital sympathectomy and microsurgical revascularization), lumbar sympathectomy, thoracic sympathectomy under video-assisted thoracic surgery. If needed, amputation of fingers or toes.
 - Antibiotic may be needed if there is infection on ulcerated skin lesions. Higher doses should be given since tissue penetration is poor in scleroderma.
2. For arthritis, non-steroidal anti-inflammatory drugs (NSAIDs).
3. Steroid and cytotoxic drugs may be used, if myositis or alveolitis.
4. Other drugs that have shown no proven benefit, but may be tried are:
 - Penicillamine—reduces cross-linking of collagen (acts as antifibrotic).
 - Methotrexate (given in a weekly dose of 7.5–15 mg).
 - Cyclosporine or interferon-γ. Recombinant human relaxin therapy (subcutaneously).
5. Other therapy, according to the involvement of the organ:
 - Physiotherapy.
 - If DPLD—cyclophosphamide or azathioprine combined with low-dose steroid.
 - Hypertension—ACE inhibitor may be given.
 - Pulmonary hypertension—oral vasodilator, warfarin and oxygen. In advanced case, prostacyclin therapy (inhaled, subcutaneous or intravenous) or oral endothelin receptor antagonist (bosentan, sitaxentan) should be given.
 - Right heart failure—symptomatic treatment with diuretic, digoxin etc. Heart lung or single lung transplantation in selected cases.
 - For reflux oesophagitis—proton pump inhibitor and prokinetic drugs.
 - For blind-loop syndrome—broad-spectrum antibiotic is useful.
 - If renal involvement—ACE inhibitor may be helpful.
 - Myositis—corticosteroid and cytotoxic drugs may be needed.

Q: What is the role of **steroid**?

A: Steroid has little or no role in the treatment of scleroderma. It can be given in low doses (10 mg/day) in DPLD due to PSS with cyclophosphamide.

Prognosis of systemic sclerosis: Depends on type, age, sex, involvement of internal organ and extent of skin involvement. Bad prognostic factors are:

- Diffuse cutaneous systemic sclerosis.
- Elderly patient.
- Male sex.
- Involvement of internal organs (especially kidney, lung and heart). Proteinuria, high ESR, low gas transfer of carbon monoxide and pulmonary hypertension.

Limited cutaneous systemic sclerosis (CRST or CREST):

- Prognosis is relatively better.
- Usually mild.
- 70% show 10-year survival.
- Pulmonary hypertension may develop later on.

Diffuse type:

- 70% show 5-year survival.
- Death due to cardiac, renal and pulmonary involvement.

Q: What are the **differential diagnoses** of systemic sclerosis or thickened skin?

A: Scleroderma-like thickening of skin, secondary to some other diseases is called **pseudoscleroderma**. The causes are:

- Scleroedema.
- Scleromyxoedema.
- Eosinophilic fasciitis or eosinophilic myalgia syndrome.
- Amyloidosis.
- Graft-versus-host disease (GVHD).
- Diabetic cheiroarthropathy.
- Acromegaly.
- Porphyria cutanea tarda.
- Carcinoid syndrome.
- Toxic oil syndrome.
- Chemically induced (pentazocine, bleomycin and vinyl chloride).

Eosinophilic Fasciitis

It is a scleroderma-like syndrome characterized by pain, swelling, and induration of skin and subcutaneous tissue followed by sclerosis of dermis and subcutaneous tissue.

- Skin is thick, but not tight.
- Common in adult, involves the skin of forearm and leg first, then peripheral parts.
- No Raynaud phenomenon and no internal organ involvement.
- Carpal tunnel syndrome is an early feature, more marked after exercise.
- It is associated with eosinophilia, hypergammaglobulinaemia, thrombocytopaenia, aplastic anaemia and myelodysplastic syndrome.

Microscopical examination of skin in eosinophilic fasciitis shows:

- Marked fibrosis of SC fascia.
- Infiltration of inflammatory cells.
- Infiltration of plenty of eosinophil.

Treatment:

- Self-limiting, spontaneous resolution may occur in 2–5 years.
- Good response to steroid.
- H_2-receptor blocker, such as cimetidine, may help.
- Diet containing L-tryptophan should be avoided.

Scleroedema

It is a disease characterized by painless, oedematous induration of face, scalp, neck, trunk and upper part of the extremities. There is no involvement of the hands and feet. Common in children, may be associated with streptococcal infection, usually self-limiting, resolves in 6–12 months.

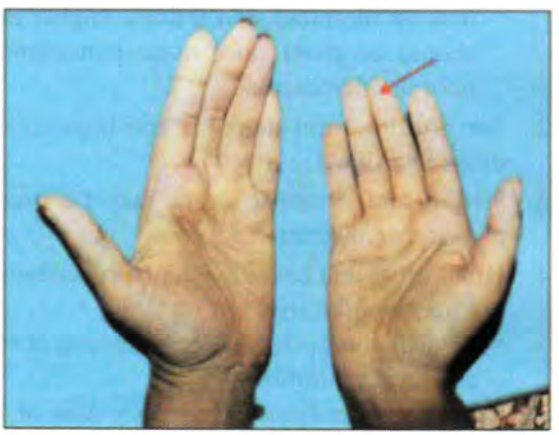
Raynaud Phenomenon or Disease

Usual instructions are:

- Look at the hand. What are the findings? What is your diagnosis?

Presentation of a Case (Hands)

- The fingers are pale, some are cyanosed and cold.
- There is sclerodactyly (tapering of fingers), infarction (or ulcer or gangrene) at the tip of finger and atrophy of pulp. May be resorption, beaking of the nails (pseudoclubbing due to resorption) and amputation of finger (may be).



Pallor on exposure to cold (palmar aspect)

Diagnosis is **Raynaud disease**.



Pallor on exposure to cold (dorsal aspect)



Infarction at the tip of fingers



Infarction at the tip of fingers, pulp atrophy

Q: What is the commonest **underlying disease**?

A: Systemic sclerosis.

Q: What is **Raynaud phenomenon**?

A: Raynaud phenomenon is a syndrome of episodic digital ischaemia manifested by pallor, cyanosis and redness of the fingers and toes on exposure to cold. Vibration and emotional activity may precipitate the attack. It is due to episodic vasoconstriction or vasospasm of small arteries, arterioles and capillaries of fingers and toes.

Q: What are the **signs** of Raynaud phenomenon? What are the **mechanisms**?

A: Three signs or stages (remember **PCR**):

- First: **P**allor (due to vasoconstriction of peripheral arterioles).
- Second: **C**yanosis (due to deoxygenated blood following ischaemia).
- Last: **R**edness (due to reactive hyperaemia, there is increased blood flow following vasodilatation).

Mechanism:

There are two theories:

- Exaggerated reflex sympathetic vasoconstriction (Raynaud original theory).
- Abnormalities in the vascular wall resulting in hyper-responsiveness and vasoconstriction to cold.
- Recent opinion suggests that accelerated destruction of platelet and release of agents such as serotonin and thromboxane A_2 have been proposed as a cause for vasoconstriction in some patients with Raynaud phenomenon.

Q: What is Raynaud **disease** and Raynaud **syndrome**? What are the **causes**?

A: As follows:

- When the disease is primary, it is called Raynaud disease.
- When the disease is secondary to other disease, it is called Raynaud syndrome.

Causes:

1. Primary or idiopathic: Also called Raynaud disease (50–60%).
 - Five times more common in females than in males.
 - Usually in young patients, 20–40 years of age, may be associated with angina.
 - Thumbs often spared. Usually runs benign course.
2. Secondary causes:
 - Systemic sclerosis (the commonest cause).
 - Collagen disease (SLE, mixed connective tissue disease [MCTD], RA, dermatomyositis and Sjögren syndrome).
 - Occupation (pneumatic drills and vibrating tools).
 - Obliterative arterial disease (atherosclerosis and Buerger disease).
 - Drugs (beta-blocker, ergotamine and cytotoxic drug: vinblastine, bleomycin and cisplatin).
 - Neurogenic (cervical rib and spinal cord disease).
 - Haematological (cryoglobulinaemia or cold agglutinin disease, myeloproliferative disease and Waldenstrom macroglobulinaemia).

Q: What are the **differential diagnoses** of Raynaud phenomenon?

A: As follows:

- Acrocyanosis.
- Erythromelalgia.
- Chilblain.
- Cold agglutinin disease.

Q: How to **treat** Raynaud disease?

A: See in systemic sclerosis.

N.B. Women who develop toxaemia of pregnancy are more likely to have history of Raynaud disease.

Rheumatoid Hand

Usual instructions are:

- Examine the hands of this patient.

Proceed as follows:

(Look at the dorsum and palm of hands, then proceed.)
Inspection: (There is bilateral, symmetrical polyarthropathy). Look carefully the following points:

1. Wasting—generalized, involving thenar, hypothenar and all the small muscles of the hand. There is dorsal guttering in both hands.
2. Any ulcer, infarction, gangrene, rash, rheumatoid nodule and palmar erythema (mention if present).
3. Joints of hands:
 - Flexion deformity or contracture.
 - PIP—spindle-shaped swelling and boutonniere deformity.
 - DIP—swan neck deformity.
 - Z-deformity of thumb, ulnar deviation and dorsal subluxation of ulna at the carpal joint.
4. Wrist joint—any swelling, synovial thickening and subluxation.
5. Ask the patient to make apposition of both hands together (prayer sign), flex and extend the fingers alternately (see any deformity).

Palpation:

1. Ask the patient, if any pain in hands (be careful not to hurt the patient).
2. Palpate the joints for tenderness.
3. Feel for rheumatoid nodule on palmar surface (head of metacarpals), dorsal surface of fingers (also seen in extensors of forearm, elbow, occiput, scapula and shin and tendo-Achilles).
4. Neurological examination of hands (see page 333 and 353).
5. Finally, assess the functional activity of hands:
 - Ask the patient to use a glass and drink, open the button, write with a pen, grip strength (ask to squeeze your fingers) and key grip (give a key, ask the patient to move the hand with the key, as in unlocking).

Q: At this point, the examiner may ask, "What else do you like to see?"

A: Yes, I want to examine other joints, eyes, chest and abdomen to see extra-articular manifestations.

Presentation of Case No. 1 (Rheumatoid Hand)

1. **Inspection:**
 - There is generalized wasting of small muscles of hands with dorsal guttering. No atrophy, ulcer, infarction, gangrene or rash.
 - Wrist joints are swollen. PIP joints of both hands are spindle shaped. There is swan neck deformity in right little and ring fingers, Z deformity in right thumb and ulnar deviation of the right hand. There is mild flexion deformity of fingers on right hand as evident by prayer sign.
 - There is dorsal subluxation of the ulnar styloid.
 - Movement is restricted in wrists and fingers of both the hands with slightly impaired functional activity.
2. **Palpation:**
 - The joints are tender.
 - Synovial thickening is present in both wrists.
 - There is a rheumatoid nodule in the extensor surface of the right forearm.

My diagnosis is **rheumatoid arthritis**.

Presentation of Case No. 2 (Vasculitis)

- Mention as above.
- There is a small ulcer and few infarctions in the tip of fingers and toes (mention which one).
- Radial pulse is feeble.

My diagnosis is **rheumatoid arthritis with vasculitis**.

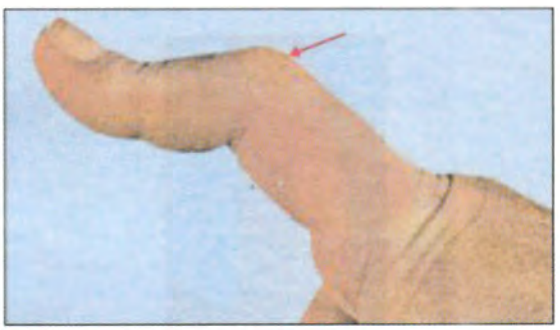
Presentation of Case No. 3 (Foot)

- All the metatarsophalangeal joints and interphalangeal joints are swollen and deformed in both feet.
- Lateral deviation with dorsal subluxation of toes.
- Plantar subluxation of the metatarsal head.
- Hallux valgus deformity.
- Feet are flat with plantar erythema.

My diagnosis is **rheumatoid arthritis**.



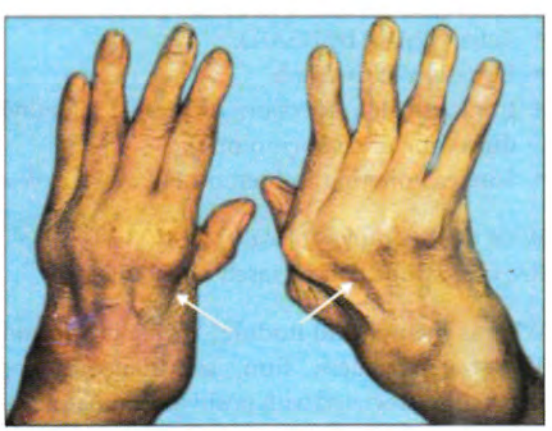
Swan neck deformity (DIP)



Boutonniere deformity (PIP)



Z-deformity of thumb, ulnar deviation and swan neck deformity



Severe rheumatoid arthritis (Dorsal guttering)



Vasculitis in rheumatoid arthritis



Vasculitis in rheumatoid hand

Q: Could it be seronegative arthritis or ankylosing spondylitis?

A: Unlikely, since in seronegative arthritis there is usually asymmetrical involvement of the bigger joints. But in my case, there is bilateral symmetrical involvement of small peripheral joints.

Q: Which joint is spared in RA?

A: Distal interphalangeal joint (may be involved in secondary osteoarthrosis).

Q: What is RA?

A: It is a chronic autoimmune inflammatory destructive and deforming polyarthritis characterized by bilateral symmetrical involvement of small and large joints, with systemic involvement and extra-articular features having a prolonged course with intermittent exacerbation and remission.

Age 30–50 years, common in females. Before menopause, it is 3 times more in female than male, but after menopause, sex ratio is almost equal.

Q: What are the mechanisms of wasting of muscles in RA?

A: Multiple factors are responsible: disuse, vasculitis, polyneuropathy, mononeuritis multiplex and entrapment neuropathy.

Q: What is **boutonniere deformity**? What is the **mechanism**?

A: Fixed flexion of PIP joint and extension of DIP joint. Because of chronic synovitis of PIP joint, there is rupture of central slip of extensor tendon, allowing to protrude the joint between two lateral slips of extensor tendon.

Q: Why it is called **boutonniere** or **button-hole**?

A: Because of rupture of central slip of extensor tendon, it looks like gap of button hole.

Q: What is **swan neck deformity**? What are the **mechanisms**?

A: Fixed flexion of DIP joint and extension of PIP joint (reverse of boutonniere).

Mechanism: Because of chronic synovitis:

- Rupture or stretching of extensor tendon on dorsum of DIP joint.
- Secondary to stretching of volar plate at PIP joint.
- Shortening of intrinsic muscles of hands, which exerts tension on dorsal tendon sheath leading to hyperextension of PIP joint.

Q: Why **radial deviation**?

A: Weakness of extensor carpiulnaris leads to radial deviation at wrist as the carpal bone rotates.

Q: Why **ulnar deviation**?

A: It occurs in response to radial deviation to keep the tendons to the phalanges in normal line to the radius.

Q: Why **Z-deformity** of thumb?

A: Because of chronic synovitis, there is hyperextension of IP joints and fixed flexion and subluxation of metacarpophalangeal (MCP) joints of thumb.



Baker cyst



Rheumatoid nodule (elbow)



Rheumatoid nodule (forearm)

Q: What is **Baker cyst**?

A: Cyst on the back of knee joint, communicates with the joints but fluid is prevented from returning to the joint by a valve-like mechanism. May rupture during knee flexion and fluid enters into the calf. After rupture, severe pain, swelling and tenderness in the calf. Confuses with deep venous thrombosis (DVT).

Diagnosis: USG of knee joint and CT scan or magnetic resonance imaging (MRI) and arthrogram.
Treatment after rupture of Baker cyst:

- Relief of pain by NSAID.
- Elevation of the limb.
- Intra-articular injection of steroid (methylprednisolone or triamcinolone).
- Surgical toileting and removal of cyst if necessary.

Q: What are the **causes** of Baker cyst?

A: RA, osteoarthrosis and rarely congenital.

Q: What is **rheumatoid nodule**? Where is it **found**?

A: These are painless, firm, subcutaneous nodule, invariably associated with positive rheumatoid factor. It is present in 20–30% cases of rheumatoid arthritis.

Sites: Pressure points such as elbow, extensor surface of forearm and hands (fingers), scapula, scalp, sacrum, shin, Achilles tendon, toes, sclera, pleura, lungs and pericardium.

Significance of rheumatoid nodule:
- It is one of the diagnostic criteria.
- Associated with high titre of rheumatoid factor (positive RA test).
- Associated with active and aggressive RA.
- A bad prognostic sign.

Histologically three zones:
- Central zone of necrotic material including collagen fibril, noncollagen filament and cellular debris.
- Mid zone of palisading macrophages.
- Outer zone of granulation tissue.

Nodules may ulcerate and become infected. Treatment with methotrexate may increase the number of rheumatoid nodule in some patients.

Nodules resolve when the disease is under control. If it causes problem, it may be removed surgically or by local injection of corticosteroid.

N.B. Rheumatoid nodules may be confused with tophi of gout, xanthomata, olecranon bursa in elbow, sarcoid nodule or neurofibroma.

Q: What are the **diagnostic criteria** of RA?

A: ARA (American Rheumatism Association) criteria:

- Morning stiffness (>1 hour).
- Arthritis of three or more joint areas.
- Arthritis of hand joints and wrist.
- Symmetrical arthritis.
- Rheumatoid nodule.
- Positive RA factor.
- Typical radiological changes (erosion or periarticular osteopaenia).
- Duration is 6 weeks or more.

N.B. When four or more criteria are present, there is 93% sensitivity and 90% specificity.

Q: What are the **bad or poor** prognostic factors of RA?

A: As follows:

1. Clinical:
 - Insidious rather than explosive onset.
 - Early development of rheumatoid nodule.
 - Extra-articular manifestations
 - Severe functional impairment.
 - One-year active disease without remission.
 - Increasing number of peripheral joints involvement.
 - Level of disability at the onset.
 - Female sex.
2. Blood tests:
 - High titres of anti-CCP antibodies and RA.
 - High CRP.
 - Normochromic normocytic anaemia.
3. X-rays:
 - Early erosive damage

N.B. Ultrasound and MRI can show cartilage and bone damage prior to conventional X-rays.

Q: What is **malignant** RA?

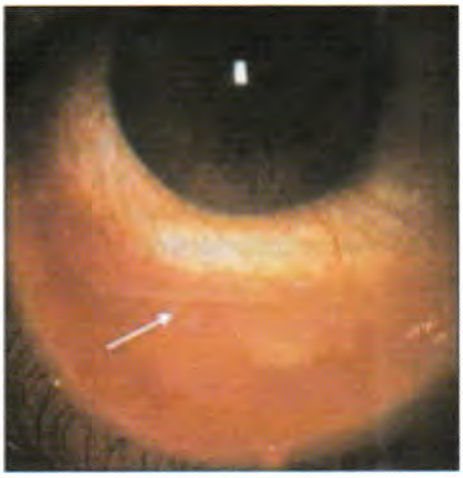
A: Severe and progressive RA associated with severe extra-articular manifestations, systemic features and vasculitis.

Q: What are the **extra-articular** manifestations of RA?

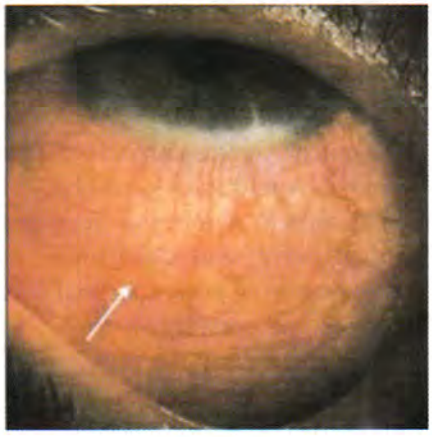
A: As follows:

1. **Eye:**
 - Episcleritis.
 - Scleritis.
 - Scleromalacia.
 - Scleromalacia perforans.
 - Keratoconjunctivitis sicca.
2. Respiratory:
 - Pleurisy.
 - Pleural effusion (may be bilateral).
 - Fibrosing alveolitis.
 - Nodules in the lungs (Caplan syndrome).
 - Obliterative bronchiolitis (rare).
3. Cardiac:
 - Pericarditis (30%).
 - Pericardial effusion (rare).
 - Chronic constrictive pericarditis (rare).
 - Rarely myocarditis, endocarditis, heart block, dysrhythmia, cardiomyopathy, aortic regurgitation and coronary artery occlusion.
4. Vasculitis: Digital arteritis and nail fold infarct, Raynaud phenomenon, visceral arteritis, mononeuritis multiplex and pyoderma gangrenosum.
5. Neurological:
 - Entrapment neuropathy (compression of nerves by hypertrophic synovium), commonly carpal tunnel syndrome (compression of median nerve) and tarsal tunnel syndrome (compression of posterior tibial nerve).
 - Peripheral neuropathy.
 - Mononeuritis multiplex.
 - Cervical cord compression (due to atlantoaxial subluxation).
 - Progressive cervical myelopathy.

6. Haematological:
 - Anaemia: Usually normocytic normochromic, occasionally macrocytic due to folate deficiency or associated with pernicious anaemia and microcytic hypochromic due to bleeding from NSAID.
 - Thrombocytosis.
 - Eosinophilia.
 - Pancytopaenia (due to hypersplenism in Felty syndrome).
7. Musculoskeletal:
 - Muscle wasting.
 - Tenosynovitis.
 - Bursitis.
 - Osteoporosis.
8. Others:
 - Lymphadenopathy.
 - Splenomegaly.
 - Osteoporosis.
 - General features (malaise, fever, weakness, loss of weight and wasting).
 - Amyloidosis.



Episcleritis



Scleritis



Scleromalacia

Q: What is **rheumatoid factor**?

A: Rheumatoid factor is an antibody, directed against Fc portion of IgG. It may be IgM or IgG type. Rheumatoid factor is positive in 75% cases, but 100% positive in RA with extra-articular manifestations. It is detected by latex slide test (RA test is more sensitive, but less specific, and is used for screening) and Rose Waaler test (RW test, the sheep cell agglutination test, is less sensitive, but more specific). Other causes of positive rheumatoid factor are:

- Collagen diseases: Sjögren syndrome (90%), SLE (30%), systemic sclerosis, dermatomyositis, fibrosing alveolitis and mixed essential cryoglobulinaemia.
- Infections: Infectious mononucleosis, infective endocarditis, tuberculosis, leprosy, kala-azar, hepatitis B, syphilis, malaria, filariasis and schistosomiasis.
- Liver disease: PBC (50%).
- Sarcoidosis.
- Temporarily after vaccination and blood transfusion.
- Over 65 years (20% in normal population).

High titres of rheumatoid factor indicate:

- Severe erosive disease.
- More extra-articular manifestations.
- Poor prognosis.
- Associated with rheumatoid nodule, vasculitis and Felty syndrome.

Q: What are the **mechanisms of anaemia** of RA?

A: As follows:

- Anaemia of chronic disorder.
- Megaloblastic anaemia (due to either folate deficiency or if associated with pernicious anaemia).
- Hypersplenism (Felty syndrome).
- Haemolytic anaemia (Coombs test may be positive).

- GIT bleeding (due to NSAID or vasculitis: causing iron-deficiency anaemia).
- Marrow suppression (gold and penicillamine, though less used nowadays).

Q: What is **palindromic** RA?

A: Recurrent acute episode of monoarthritis lasting 24–48 hours. Knee and finger joints are most commonly affected, but any peripheral joint may be involved. Fever may occur, but no other systemic features. It may be confused with acute gouty arthritis and atypical onset of rheumatoid arthritis. There may be many attacks without any permanent articular damage. However, one-third to half cases may develop typical RA. This can be treated with NSAID during pain. Hydroxychloroquine may be used in preventing recurrent attack.

Q: What is **Caplan syndrome**?

A: Rheumatoid lung nodules with pneumoconiosis is called Caplan syndrome. Common in coal-workers' pneumoconiosis, may occur in any pneumoconiosis. Nodules are rounded, 0.5–2.5 cm, present at periphery of the lung. These may rupture causing pneumothorax or may cavitate and cause haemoptysis. It may be confused with tuberculosis or neoplasm.

Q: What is **Felty syndrome**?

A: Rheumatoid arthritis with splenomegaly and neutropaenia is called Felty syndrome. There may be hypersplenism (anaemia, leucopaenia and thrombocytopaenia). It occurs in long-standing, seropositive, deforming, but inactive arthritis, in <1% of the cases. Females are affected more than males, age 50–70 years. Leg ulcers or sepsis are complications due to nutropaenia. Splenectomy may be necessary for hypersplenism. It is associated with high titre of rheumatoid factor, subcutaneous nodules and other manifestations of systemic rheumatoid disease.

Q: What precaution is necessary before **general anaesthesia or upper GI endoscopy**?

A: X-ray of the cervical spine should be taken to rule out atlanto-axial subluxation. (Otherwise during anaesthesia, cervical cord compression may lead to sudden death).

Q: If the patient develops **nephrotic syndrome** (or proteinuria in urine examination), what is the likely cause?

A: Renal amyloidosis.

Q: What are the **investigations** done in RA?

A: As follows:

- FBC (ESR is high, pancytopaenia may occur in Felty syndrome).
- RA test and RW test.
- Anti-CCP antibody (cyclic citrullinated peptide).
- X-ray of hands and other involved joints, chest X-ray.
- Others: CRP (high) and urine analysis (proteinuria, may occur in amyloidosis).

Q: What is **anti-CCP antibody**? What is its **significance**?

A: It is the antibody to cyclic citrullinated peptide (CCP). It binds to peptides in which the amino acid arginine is converted to citrulline by peptidylarginine deaminase, an enzyme abundant in inflamed synovium.

Anti-CCP antibody is highly specific in RA (95%), present in 70% patients with rheumatoid arthritis. Unlike rheumatoid factor, it is not positive in other autoimmune diseases. It is helpful for early diagnosis and is also a predictor of an aggressive disease. In patient with undifferentiated arthritis, anti-CCP antibody is helpful for early diagnosis of RA. It may be detected in asymptomatic patient several years before the development of RA.

Q: How to **treat** RA?

A: As follows:

- Relief of symptoms by rest and NSAID. Also intra-articular injection, splinting, hydrotherapy etc. may relieve symptoms.
- Suppression of activity and progression of disease by disease modifying antirheumatic drug (DMARD).
- Other measures: Physiotherapy, orthopaedic measures. Synovectomy of the wrist or finger tendon sheaths of the hands may be required for pain relief or to prevent tendon rupture when medical interventions have failed. Osteotomy, arthrodesis or arthroplasty may be needed later.
- Patient education is important.

Q: What are the **surgical** treatments in RA?

A: As follows:

- Synovectomy of wrist or finger tendon sheath (for pain relief or tendon rupture).
- In advanced or severe cases, arthrodesis, arthroplasty and osteotomy may be done in selected cases.

Q: What **DMARDs** are used?

A: As follows:

- First choices are sulphasalazine and methotrexate.

- Other drugs: Chloroquine, hydroxychloroquine, leflunomide, azathioprine, and cyclosporine (gold and penicillamine are not used any more).
- Anti-TNF-alpha and IL-1, also rituximab, are more effective than other DMARD in preventing joint erosions. If disease activity persists despite an adequate trial of two DMARDs, anti-TNF therapy should be considered.

DMARD should be started from the beginning, may take 4–12 weeks for response. If no effect in 6–12 weeks, combination with methotrexate and sulphasalazine may be given. Prednisolone 7.5–10 mg may be added with DMARD to give symptomatic relief.

Brief note about DMARDs:

Sulphasalazine:

1. When taken by mouth, it is broken to sulphapyridine and 5-aminosalicylic acid (ASA). Sulphapyridine is effective in RA (ASA is effective in inflammatory bowel disease). It acts probably by inhibiting cyclo-oxygenase and other enzymes responsible for synthesis of prostaglandin.
2. Dose: Start with low dose, increase the dose weekly.
 - Initially, 250 mg (½ tablet) BID for 1 week.
 - Then 500 mg (1 tablet) BID for 1 week.
 - Then 1,000 mg (2 tablets) BID to be continued (maximum dose 2–3 g daily).
3. Side effects: GIT upset (anorexia, nausea, vomiting, diarrhoea), skin rash, Stevens–Johnson syndrome, reversible sterility in males, blood dyscrasias (agranulocytosis, megaloblastic anaemia and haemolytic anaemia).
4. Periodic check up: FBC, liver function test (SGPT) and renal function tests (creatinine), every 1–3 months.

Methotrexate:

- Very effective DMARD. May take 4–6 weeks to act.
- Dose: 7.5–10 mg, in a fixed day weekly (up to 25 mg). Folic acid 5 mg/day should be given on the next day (folinic acid is more preferable).
- Side effects: Anorexia, nausea, vomiting (prevented by using anti-emetic before starting the drug). Rarely, may cause bone marrow depression. Prolong use may cause hepatic fibrosis and DPLD.
- Periodic check up: CBC, liver function tests (SGPT) and renal function test (creatinine) should be done.
- Mechanism of action: Competitively inhibits dihydrofolate reductase, interfering with DNA synthesis and cell division.

Chloroquine:

- It is a weak with slow DMARD effect.
- Dose: 250 mg daily as a single dose.
- Side effects: Anorexia, nausea, vomiting, skin rash. Prolonged use may cause neuromyopathy and ocular toxicity. In eye, corneal microdeposit (reversible after drug withdrawal), retinopathy (may cause blindness), bull's eye macula and optic neuritis.
- Periodic examination of eye is essential. To reduce ocular toxicity, the drug can be given for 10 months in a year.

Hydroxychloroquine:

- Dose: 200–400 mg daily.
- Used alone in mild disease or as an adjuvant with other DMARD.
- Retinopathy is the serious complication, but this is rare before 6 years of treatment.

Leflunomide:

- It can be used if methotrexate fails to respond. Also can be used together with methotrexate.
- Dose: 100 mg daily for 3 days, then 10–20 mg daily.
- Side effects: Skin rash, diarrhoea, reversible alopecia, hepatotoxicity, carcinogenic and teratogenic. It needs a washout of 2 years before conception (3 months in man and 2 years in woman), so avoid in women who want to be pregnant.
- Periodic blood check up is mandatory.

Biological agents:

These agents block specific immune factors responsible for RA. Drugs are anti-TNF-alpha and IL-1 receptor antagonist. These are highly expensive, used only when there is failure of two DMARDs.

Anti-TNF-alpha:

1. It is more effective, rapid onset of action, greater clinical efficacy and sustained benefit than standard DMARD.
2. Anti-TNF drugs are:
 - Infliximab (given in infusion every 1–2 months)
 - Etanercept (given SC every 2 weeks)
 - Adalimumab (given SC every 2 weeks)
3. Common side effects: Hypersensitivity reaction, headache, hypotension. Reactivation of latent tuberculosis may occur. Sometimes lymphoma may occur.

Anti-interleukin (IL-1) receptor:

- Anakinra may be used in RA when anti-TNF-α is unsuccessful (less effective than anti-TNF). It is used in combination with methotrexate.

Anti-interleukin 6 (IL-6) receptor:

- Tocilizumab: It is a humanized monoclonal antibody against IL-6 receptor. It is used for treatment of moderate to severe active rheumatoid arthritis in adult patient, alone or in combination with methotrexate and/or other DMARDs. Dose 8 mg/kg as IV infusion, once in every 4 weeks.

Rituximab:

- It is an antibody directed against the CD-20 receptor, expressed on B lymphocytes.
- It produces significant improvement in RA positive patients. May be used alone or in combination with steroid or methotrexate.
- It is given by two IV infusions (1 g each) 2 weeks apart.

Tocilizumab:

- It is an antibody directed against the IL-6 receptor.
- It acts similar to those of TNF blockade.

Q: What are the **criteria for remission or response to therapy** of RA?

A: As follows:

- No joint pain
- No fatigue
- No joint tenderness
- Morning stiffness <15 minutes.
- No soft tissue swelling.
- ESR less than 30 mm in 1st hour.

At least 5 criteria must be present for at least 2 consecutive months.

Q: What are the **differences** between rheumatic fever and rheumatoid arthritis?

A: As follows:

Points	Rheumatic fever	RA
Age	5–15 years	20–40 years
Cause	Sequelae of immune response to *Streptococcus* beta-*haemolyticus* sore throat	Autoimmune
Joints	Large	Peripheral small joints
Type of arthritis	Fleeting	Bilateral, symmetrical
Diagnosed by	Two major or one major and two minor criteria plus signs of previous *Streptococcus* infection	Four of seven criteria
Morning stiffness	Absent	Present
RA test	Negative	Positive
Subcutaneous nodule	Present	Rheumatoid nodule
Erythema marginatum	Present	Absent
Joint deformity	Absent	Present
Cardiac involvement	Common	Less
Chronic constrictive pericarditis	Never	May cause
Chorea	May be present	Absent
Treatment	Prophylactic penicillin	DMARD
Sequelae	Rheumatic valvular lesion (it licks the joints, kills the heart)	Not so

Q: What is **Sjögren syndrome**? How will you **confirm** it?

A: It is an autoimmune disorder characterized by dryness of eye (keratoconjunctivitis sicca) and dryness of mouth (xerostomia) with nonerosive arthritis. Fibrosis and atrophy of the salivary glands occur. There is infiltration of lymphocytes and plasma cells in lacrimal and salivary glands. It is of two types:

- Primary: Not associated with collagen disease (sicca syndrome).
- Secondary: Associated with collagen disease (commonly RA).

Presentation of primary Sjögren syndrome:
common in females, F:M = 9:1, 40–50 years.

- Dryness of mouth and eyes.
- Arthralgia and non-progressive arthritis.
- Raynaud phenomenon.
- Dysphagia.
- In lung—pulmonary diffusion defect and fibrosis.
- Renal (renal tubular acidosis, nephrogenic diabetes insipidus).
- Vasculitis.
- Others (fever, weakness, lymphadenopathy and neuropathy, fit, depression).

- Lymphoma—increased incidence of non-Hodgkin B cell lymphoma. (It is associated with 40-fold risk).
- May be associated with other autoimmune disease like thyroid disease, myasthenia gravis, PBC, autoimmune hepatitis.

Investigations:

1. CBC (high ESR).
2. Schirmer test (a strip of filter paper is placed inside lower eyelid. In normal people, at least 6 mm is wet in 5 minutes. In Sjögren syndrome <5 mm).
3. Biopsy of lip or salivary gland (lymphocytic and plasma cell infiltration).
4. Rose Bengal staining of eyes shows punctate or filamentary keratitis.
5. Antibody test:
 - RA test (positive in 90%).
 - ANA (positive in 60–70%).
 - Anti-Ro (SS-A, positive in 70%. It can cross placenta causing congenital complete heart block).
 - Anti-La (SS-B).

Treatment:

- Artificial tear (hypromellose), contact lens, oral hygiene, artificial saliva, oral gel and chewing gum.
- Stimulation of saliva flow by sugar-free chewing gum or lozenges may be helpful.
- Oral candidiasis should be treated promptly.
- Vaginal dryness is treated with lubricants such as K-Y jelly.
- Hydroxychloroquine (2–3 mg/kg daily, may improve the flow of tear).
- Treat the primary cause.
- Extraglandular and MSK manifestations may respond to steroid. Immunosuppressive drugs can be added.

Knee Joint Arthritis (Examination of Knee Joint)

Usual instructions are:

- Examine the knee joints.
- Examine the lower limbs. What are your findings?

Proceed as follows:

(With permission, expose the knee and thigh, the patient is lying in a supine position. Look carefully both front and back of the knee.)

Inspection:

- Obvious joint swelling (right or left, localized or generalized).
- Deformity of the joint.
- Skin (red, shiny, pigmentation and scar mark).
- Back of knee (Baker cyst).
- Wasting of muscles of thigh or leg, swelling in calf (rupture Baker cyst).

Palpation:

- Feel the temperature (compare with normal side).
- Tenderness.
- Synovial thickening (suprapatellar part).
- Examine for effusion:
 - Patellar tap (fluid from suprapatellar bursa is forced in joint space by squeezing the lower part of quadriceps; then patella is pushed posteriorly by tip of two or three fingers).
 - If small effusion, see **Bulge sign** (as follows: left hand compresses the suprapatellar pouch at the lower end of quadriceps and the finger of right hand is run along the groove on either side of patella alternately; bulging, if present due to small effusion, will not be compressed).
- See the movement slowly and passively, ask if there is any pain. See the range of movement and feel for crepitus.
- Now examine the ligaments:
 - Medial and lateral collateral ligaments: By just flexing the knee and holding the leg with one hand, palpate with other hand in lateral and medial movement of leg.
 - Cruciate ligaments: Flex the knee at 90°, then sit over the foot of the patient lightly to fix the leg. Now pull and push the leg anteriorly and posteriorly by keeping the fingers on the back of knee and feel the ligaments. Increased anterior movement of the leg suggests anterior ligament laxity, and increased posterior movement of leg suggests posterior ligament laxity.

N.B. If asked to examine the lower limbs and if obvious finding is arthritis, then examine the joints mainly. If nothing obvious, perform the neurological examination.

Presentation of a Case (Painful Left Knee Joint with Effusion): Case No. 1

- The left knee joint is swollen, more marked above the patella.
- Skin is red and shiny.
- There is a cystic swelling on the back of right knee (Baker cyst).
- Local temperature is raised, and the joint is tender.
- Patellar tap is positive (indicates effusion).
- There is restricted movement on left knee.

My differential diagnoses are (mention the causes according to age):

In young patient, the causes are:

- Traumatic.
- Infective arthritis (pyogenic and tuberculous).
- Juvenile idiopathic arthritis (JIA).
- Reactive arthritis or Reiter syndrome.
- Haemophilic arthritis.
- Other seronegative arthritis (ankylosing spondylitis and psoriatic arthritis).

In middle aged or elderly patient, the causes are:

- Traumatic.
- Infective arthritis (pyogenic and tuberculous).
- Gout.
- Pseudogout.
- Reactive arthritis.
- Osteoarthrosis.
- RA.



Knee swelling (left)



Knee swelling (bilateral)

Presentation of a Case (Painful Knee Joint, Both Knee Joints): Case No. 2

- Describe as above in both knee joints.

My differential diagnoses are (mention according to the age):

In young patient, the causes are:

- Rheumatic fever (if deformity, it is **against** rheumatic fever).
- Reactive arthritis or Reiter syndrome.
- JIA.
- Seronegative arthritis (ankylosing spondylitis and enteropathic arthritis).
- Rheumatoid arthritis.
- Psoriatic arthritis (check for skin lesion and nail change).

In middle aged or elderly patient, the causes are:

- Osteoarthrosis.
- Gout.
- Pseudogout.
- Rheumatoid arthritis.
- Psoriatic arthritis.
- Seronegative arthritis (ankylosing spondylitis and enteropathic arthritis).

Q: How will you **investigate** this patient?

A: As follows:

1. FBC: Leucocytosis (septic arthritis) and high ESR.
2. X-ray of knee joint.
3. RA test.
4. Serum uric acid.
5. Aspiration of joint fluid and analysis:
 - Physical character (straw, purulent and haemorrhagic).
 - Gram staining and cytology.

- Biochemistry (protein and sugar).
- C/S.
- Acid-fast bacillus (AFB).
- If gout suspected, uric acid crystal (to be seen under polarising light).

6. Others:
 - Blood for C/S (if septic arthritis).
 - If SLE suspected (ANF, anti-double-stranded DNA).
 - Synovial biopsy.

Read the Following Topics in Relation to Arthritis

Q: What are the **causes of acute monoarthritis**?

A: As follows (remember the mnemonic: **GRASP-TH**):

- **G:** Gout.
- **RA:** Reactive arthritis.
- **S:** Septic arthritis (pyogenic).
- **P:** Pseudogout.
- **T:** Trauma, tuberculous.
- **H:** Haemophilia (in early age).

N.B. In children, septic arthritis and JIA are the common causes. Also, haemophilic arthritis, leukaemia and osteomyelitis may occur.

Q: What are the **causes of polyarthritis**?

A: As follows:

1. Infective (bacterial and viral).
2. Inflammatory:
 - Rheumatic fever.
 - RA and its variants.
 - Seronegative arthritis (ankylosing spondylitis, Reiter syndrome, enteropathic arthritis and psoriatic arthritis).
 - JIA (<16 years). Collagen disease (SLE, dermatomyositis, systemic sclerosis and polyarteritis nodosa).
3. Degenerative (osteoarthrosis).
4. Metabolic (gout, pseudogout).
5. Neuropathic arthropathy (Charcot joint).
6. Haematological (haemophilic arthritis and Henoch–Schönlein purpura).
7. Others (polymyalgia rheumatica, sarcoidosis, haemochromatosis, acromegaly and hypertrophic osteoarthropathy).

N.B. In any patient with mono- or polyarthritis, history of annular skin rash, facial palsy, diagnosis may be Lyme disease.

Q: What are **oligoarthritis and polyarthritis**?

A: As follows:

- When there are less than five joints or joint groups are involved, it is called oligoarthritis (pauciarticular arthritis)
- When more than five joints or joint groups are involved, it is called polyarthritis.

Q: What is **Charcot joint**? What are the **causes, features and treatment**?

A: It is a chronic progressive degenerative arthropathy characterized by deformity, osteoarthrosis and new bone formation, resulting from disturbance of sensory innervation of affected joint. Causes are:

- Diabetes mellitus (usually involves the joints of foot).
- Tabes dorsalis (usually involves the joints of lower limbs—knee, ankle and hips).
- Syringomyelia (usually involves joints of upper limbs—elbow, wrist and shoulder).
- Others: Meningomyelocele, repeated intra-articular injection of steroid, leprosy and amyloidosis.

Features:

- Painless joint with deformity.
- Enlargement of joint with bony outgrowth.
- May be effusion.
- Loose body.
- Joint (unstable, subluxation and crepitus).

Treatment:

- Treatment of primary cause.
- Braces and splints may be used.

Differences between mechanical and inflammatory arthritis

Features	Mechanical arthritis	Inflammatory arthritis
Age	Any	Below 40 years
Onset	Acute	Insidious, >3 months
Family history	Absent	Usually positive
Exercise	Worse	Improved
Rest	Better	Worse
Morning stiffness	Absent	Present
Sleep disturbance	Absent	Present
Neurological signs	May be present	Absent

Range of movement	Asymmetrical	Symmetrical
Straight leg raising (SLR)	Positive	Normal
Swelling and warm	Absent	Present

Maximum pain	After movement	After rest
Crepitus in joint	Coarse crepitus	Fine crepitus
ESR and CRP	Normal	High

Juvenile Idiopathic Arthritis (JIA/JCA)

Usual instructions are:

- Examine the legs or knee joints (patient is usually a child or young adult).

Presentation of a case: (as described previously in knee joint)

Q: What are your **differential diagnoses**?

A: As follows:

- Rheumatic fever.
- Seronegative arthritis.
- SLE.
- Viral arthritis.
- Acute leukaemia.

Q: What **relevance** do you like to see?

A: As follows:

- I want to examine other joints and also spine.
- For systemic onset JIA (Still disease): Hepatosplenomegaly, lymphadenopathy, erythematous skin rash (present during fever called **Salmon rash**), pleurisy, pericarditis and eye (to see iritis).
- Detailed history to exclude other causes of arthritis in children.



Deformity in elbow and small chin in JIA



Spindle-shaped PIP in JIA



Deformity in knee and joints of upper limbs in JIA



Deformity of joints in hands in JIA



Swollen knee joint in JIA



Salmon rash in JIA

Q: Could it be **rheumatic fever**?

A: Unlikely, because in rheumatic fever, there is no deformity of joints and wasting of muscles. Moreover, rheumatic fever is diagnosed by major and minor criteria (rheumatic fever licks the joints and kills the heart).

Q: Why is there **wasting** of muscles in JIA?

A: Disuse and release of cytokines (interleukin 1, 6 and TNF).

Q: What are the **causes of acute arthritis in children**?

A: As follows:

- Rheumatic fever.
- JIA.
- Infections (bacterial and viral).
- Acute leukaemia.
- Henoch–Schönlein purpura.
- Haemophilic arthritis.
- Reactive arthritis.
- Others are sickle cell disease, psoriatic arthritis, SLE, osteomyelitis and hypermobility syndrome.

Q: What **investigations** should be done in JIA?

A: As follows:

- Complete blood count (leucocytosis in Still disease, may be lymphocytosis, thrombocytosis and high ESR).
- CRP (high).
- RA test (usually negative, positive in 10% cases).
- ANA, Anti–ds-DNA if SLE is suspected.
- X-ray of the involved joint.
- Other investigations to exclude other diseases (according to history).

Q: What is **JIA**?

A: It may be defined as onset of arthritis before 16 years of age and persisting for more than 3 months.

Q: What are the **types** of JIA?

A: As follows:

1. Systemic onset (**Still disease**)—10–15% cases.
2. Oligoarthritis (pauciarticular): It is of 2 types:
 - Oligoarthritis(persistent):Common(50–60%), four or less joints are affected, mainly knee, ankles and wrists, in asymmetrical pattern. Common in girls, 3 years of age. Uveitis may occur. Relatively good prognosis.
 - Oligoarthritis (extended): Occurs in 25% cases, arthritis of many joints may develop after 6 months. This can be very destructive.
3. Polyarticular JIA: Involvement of more than four joints, 30–40% cases of JIA. It is of two types.
 - RA test is positive: Affects girls older than 8 years. Small joints of hands, wrist, ankle, feet etc. are involved; later larger joints are involved. Can be very destructive.
 - RA test is negative: Affects more in girls younger than 12 years, but may be in any age. Joints involvement like RA positive type but cervical spine, temporomandibular joint and elbows may be involved. ANA may be positive with chronic uveitis.
4. Other types of juvenile arthritis:
 - Enthesitis-related JIA.
 - Psoriatic arthritis.
 - Unclassified.

Q: What are the **features** of systemic onset JIA (Still disease)?

A: As follows:

- Arthritis: Involving knee, wrist and ankle. Other joints may be involved.
- High fever: Intermittent type, may be continuous.

- Skin rash: Appears with fever and disappears when fever subsides. These are macular or maculopapular, Salmon pink colour rashes (**Salmon rash**).
- Extra-articular features: Hepatosplenomegaly and lymphadenopathy (common). There may be pericardial effusion, pleural effusion and disseminated intravascular coagulation (DIC).
- In chronic cases: Micrognathia (small mandible), fusion of cervical spine, and retardation of growth.

Q: How to treat JIA?

A: As follows:

1. To relieve pain, NSAID.
2. General measures:
 - Rest during pain and passive movement of the limb to prevent contracture.
 - Physiotherapy.
 - Explanation and reassurance to the parents, also to the patient.
3. In severe cases: Steroid, preferably alternate days. Pulse methylprednisolone may be given, followed by methotrexate (steroid may cause early fusion of epiphysis resulting in short stature. Even 3 mg prednisolone daily may cause this effect.)
4. Disease modifying drugs should be given in all cases:
 - Methotrexate—5 mg weekly (increase the dose gradually).
 - Sulphasalazine—30–50 mg/kg, effective in enthesitis related JIA.
 - Others—IV immunoglobulin, cyclosporine and cytotoxic drugs (cyclophosphamide, chlorambucil and azathioprine) may be tried.
 - If methotrexate fails, anti-TNF may be given (helpful in all cases, except in systemic onset type, where results are variable). Etanercept may be used.
5. Orthopaedic surgery, if needed.

N.B. If aspirin is used for fever or arthritis, associated with viral infection like influenza below 12 years of age, it may cause Reye syndrome. So, it should be avoided.

A Brief Note on Adult Still Disease

It is a disease of unknown cause, characterized by high fever, seronegative arthritis, skin rash and polyserositis. Usually, it is diagnosed by exclusion of other diseases. Commonly occurs in young adults between 16 and 35 years of age, rarely after 60 years.

Diagnostic criteria of Adult Still disease:

Each of the 4 criteria:

- Quotidian fever, more than 39°C.
- Arthralgia or arthritis (knee, wrist and ankle).
- Rheumatoid factor is negative.
- ANF is negative.

Plus 2 of the following:

- Leucocytosis >15 × 10^9/L (usually very high, may be >40,000).
- Evanescent macular or maculopapular rash, Salmon coloured, nonpruritic (common in chest and abdomen).
- Serositis (pleurisy or pericarditis).
- Hepatomegaly.
- Splenomegaly.
- Lymphadenopathy (usually cervical, may be generalized).

High fever with chill and sweating is very common. Initially, arthritis may be mild. Other features—abdominal pain, myalgia and sore throat.

Investigations:

- CBC (low haemoglobin, high ESR and leucocytosis).
- CRP (is high).
- RA and ANF (are negative).
- Serum ferritin is very high (>10,000).
- Fibrinogen level (high).
- AST and ALT (high).

Treatment:

- NSAID (high-dose aspirin 1 g 8 hourly). Other NSAIDs—indomethacin, ibuprofen may be helpful. NSAID may be effective in 50% cases.
- If no response—high-dose prednisolone (60–100 mg/day). When the fever subsides, reduce the dose slowly. Steroid is necessary in 50% cases.
- Other drugs—chloroquine, hydroxychloroquine, methotrexate, sulphasalazine, azathioprine and cyclophosphamide may be tried.
- In chronic case, tumour necrosis factor (TNF) antagonists such as etanercept or anakinra (interleukin-1 receptor agonist) may be considered.

N.B. Recurrent episode occurs in one-third cases.

Septic Arthritis

Usual instructions are:

- Examine the legs or knee joints.

Presentation of a case: (present as in knee joint arthritis)

Q: What are the **differential diagnoses**?

A: See in monoarthritis in knee joint arthritis (mention the causes according to the age of the patient).



Septic arthritis

Q: What are the **causes** of septic arthritis?

A: As follows:

- Haematogenous spread from skin or other site of infection.
- Direct puncture or joint aspiration or trauma.

Q: What are the **risk factors** for septic arthritis?

A: As follows:

- Pre-existing joint disease (e.g. RA).
- DM.
- Immunocompromised state.

Q: What are the **presentations** of septic arthritis?

A: As follows:

1. Features of joints:
 - Severe acute or subacute monoarthritis, may be polyarthritis (if there is septicaemia).
 - Joint is swollen, hot and red with severe pain and restricted movement.
2. Systemic features: High fever, malaise and weakness.

Q: What are the **investigations** done in septic arthritis?

A: As follows:

- CBC (leucocytosis).
- CRP.
- Blood C/S.
- X-ray of the joint involved.
- Joint fluid aspiration: See the physical character (turbid), biochemistry, cytology (>5,000/mm^3), Gram staining and C/S.

Q: How to **treat septic arthritis**?

A: As follows:

- Complete rest.
- For pain, give NSAID.
- Antibiotic mainly flucloxacillin (2 g IV 6 hourly) for 2–3 weeks, then oral (9–10 weeks). Other antibiotic may be added.
- Joint aspiration may be necessary. Occasionally, surgical drainage.
- Early regular passive movement.

Q: What are the **causes** of infective arthritis?

A: As follows:

- Bacterial: *Staphylococcus aureus* (causing native arthritis), *Staph. epidermidis* (prosthetic arthritis), *Streptococcus*, *Pneumococcus*, *Meningococcus*, *H. influenzae* etc.
- Viral: Parvovirus B19, rubella, HBV, HIV.
- Gonococcal arthritis: There is purulent arthritis (may be fleeting) associated with pustular skin lesion, tenosynovitis, urethral discharge and history of sexual exposure.
- Tubercular arthritis. One specific of tubercular arthritis is called Poncet disease, which is associated with tenosynovitis and arthritis.
- Lyme disease: Caused by *Borrelia burgdorferi* from the bite of infected tick. Initially, there is skin rash called erythema chronicum migrans accompanied by fever, malaise, headache, arthralgia, lymphadenopathy. After weeks or months, some patients develop features of meningoencephalitis, cranial or polyneuropathy, cardiac problem like conduction block, myocarditis and arthritis. Confirmed by detection of antibody titre—IgM in the first month, IgG in later months. Amoxicillin or doxycycline is given early in the disease. Late disease should be treated with IV ceftriaxone or benzyl penicillin for 2–4 weeks.

Haemophilic Arthritis

Usual instructions are:

- Examine the legs or knee joints.

Presentation of a Case (Patient is a Child or Young)

1. **Inspection:**
 - Both knee joints are swollen, erythematous and deformed, right one more than the left.
 - Muscle wasting is present around both knee joints, more over the right knee.
 - There are few ecchymosis of various sizes over the right thigh.
2. **Palpation:**
 - Both knee joints are warm and tender.
 - Patellar tap is positive.
 - Movement is restricted.

My **differential diagnoses** are:

- Juvenile idiopathic arthritis (JIA).
- Rheumatic fever.
- Haemophilic arthritis (due to haemophilia A).
- Christmas disease with arthritis.
- Acute leukaemia.
- Septic arthritis.

Q: Ask one history to the patient.

A: I would like to ask any history of prolonged bleeding following any trauma, injury or tooth extraction.

Q: Can it be **rheumatic fever?**

A: It can be. It is diagnosed by major and minor criteria.

Q: Which **joints** are **commonly involved** in haemophilic arthritis?

A: Commonly knee, elbow, ankle and hip joints are involved.

- In infants, hip joint is commonly involved.
- In older children, knee joint is commonly involved.





Haemophilic arthritis (knee joint)

Q: What is the **cause of joint deformity** in haemophilia?

A: It is due to secondary osteoarthrosis and wasting of the muscles around the joint.

Q: What are the **presentations** of haemophilic arthritis?

A: Haemarthrosis occurs when plasma level of factor VIII-C is <1%. Arthritis may be spontaneous without trauma or may follow even minor trauma.

- Initially, tingling, abnormal sensation, stiffness and instability of the joint.
- Later on, the joint is red, hot, swollen and painful.

Progression of arthritis depends on repeated haemarthrosis, which leads to:

- Synovium hypertrophy.
- Fibrotic change in synovium.
- Destruction of cartilage.
- Reduction of joint space.
- Subchondral cyst formation.
- Bone shows erosion, marginal sclerosis, osteophyte formation and ankylosis of joint.

Q: What are the **radiological signs** in haemophilic arthritis?

A: As follows:

- Initially, joint space is increased and widening of intercondylar notch occurs (in knee joint, indicates long-standing haemorrhage).
- Later on reduction of joint space, periarticular osteopaenia, marginal sclerosis, subchondral cyst formation, secondary osteoarthrosis (with osteophyte) and ankylosis of joint.





Haemarthrosis in haemophilia (wide intercondylar notch and joint space)

Q: What are the **causes of haemarthrosis?**

A: As follows:

- Trauma.
- Haemophilia.
- Christmas disease.
- Von Willebrand disease.
- Sickle cell disease.
- Excess anticoagulant.
- Rarely, malignancy.

Q: How to **treat** haemophilic arthritis?

A: As follows:

- Complete rest, elevation of the affected limb and immobilization by splinting.
- Analgesic may be given (paracetamol or acetaminophen or codeine). Aspirin or other NSAIDs are contraindicated (as they interfere with platelet function and may cause excess bleeding).
- Factor VIII transfusion 20–30 IU/kg. Repeated after 12 hours and also after 24 and 36 hours (higher dose is required, if treatment is delayed).
- Once acute stage is over, the patient should be mobilized, and physiotherapy should be started (isometric exercise, followed by active movement, hydrotherapy).
- Arthrocentesis (aspiration from joint) is rarely necessary.

Q: What is **haemophilia?**

A: It is an X-linked inherited disorder due to deficiency of factor VIII or antihaemophilic factor, characterized by prolonged bleeding. Usually, female is the carrier and male is the sufferer. There is high rate of new mutations, in 30% there is no family history.

Q: What are the **types** of haemophilia?

A: Normal factor VIII level is 50–150 IU/dL. According to severity, it is of 3 types:

- Mild—Factor VIII is >5 IU/dL (bleeding occurs following major injury or surgery).
- Moderate—Factor VIII is 1–5 IU/dL (bleeding occurs following minor injury or surgery).
- Severe—Factor VIII is <1 IU/dL (spontaneous bleeding into the joints, muscles).

Q: What is the **pedigree** of haemophilia?

A: As follows:

1. If father is affected:
 - All daughters are carriers.
 - All sons are normal.
2. If mother is carrier:
 - 50% daughters are carriers.
 - 50% sons are sufferers.

N.B. Remember the following points:

- In female carrier, 1 son is affected, 1 son is normal, 1 daughter is carrier and 1 daughter is normal.
- In a female carrier, factor VIII is <50% normal, because of randomized inactivation of one X-chromosome.

Q: Can a **female** be the **sufferer** in haemophilia?

A: Yes, rarely a female can suffer, because of the following reasons:

- If her mother is a carrier and father is a sufferer of haemophilia.
- Turner syndrome (45 XO).
- According to lyonization theory, there is randomized inactivation of one X chromosome in the developing fetus. Then the number of affected X chromosome may be predominant. Female may be affected, if normal X chromosome is disproportionately inactivated.

Q: How does a patient with haemophilia usually present?

A: Depends on whether factor VIII deficiency is mild, moderate or severe.

- Prolonged and persistent bleeding after trauma or injury, tooth extraction.
- Sometimes, spontaneous bleeding may occur in severe cases.
- Bleeding into the large joints and muscles (psoas and calf muscle) is also common.

Q: What is the common site of **muscular bleeding**?

A: Commonly in calf muscles and psoas.

Q: What happens if the patient has **bleeding into the psoas** muscle?

A: As follows:

- Severe pain in lower abdomen.
- Paraesthesia in thigh and weakness of quadriceps due to compression of femoral nerve.

Q: What **investigations** are done in haemophilia?

A: As follows:

- FBC, platelet (usually normal).
- Bleeding time (normal).
- Prothrombin time (normal).
- Clotting time (prolonged).
- APTT (prolonged).
- Factor VIII:C assay (deficient or absent).
- vWF (normal).
- Serum fibrinogen (normal).
- X-ray of involved joint (in haemophilic arthritis).

N.B. APTT is prolonged, which is corrected by addition of normal plasma. If not corrected after the addition of normal plasma, more likely there is antibody formation or the presence of antiphospholipid antibody.

Q: Is **antenatal diagnosis** possible?

A: Yes. Antenatal diagnosis may be done by molecular analysis of fetal tissue obtained by chorionic villus biopsy at 11 to 12 weeks of pregnancy.

Q: How will you **manage haemophilia**?

A: As follows:

1. Management of bleeding episode:
 - Factor VIII concentrate is given by intravenous infusion, twice daily as its half-life is 12 hours and the blood level should be maintained for 3–5 days.
 - For minor bleeding, factor VIII level should be raised to 20–30 IU/dL. However, desmopressin 0.3 microgram/kg 12 hourly infusion over 20 minutes may be given, which raise factor VIII.
 - For severe bleeding, factor VIII level should be raised to at least 50 IU/dL. Treatment to be continued for a period of 1 week or more.
 - For major surgery, factor VIII level should be raised to 100 IU/dL preoperatively and maintained above 50 IU/dL until healing. Continuous infusion may be needed. Treatment to be continued for 7–10 days.
2. If factor VIII is not available, cryoprecipitate, fresh frozen plasma or fresh blood can be given.
3. To prevent recurrent bleeding into joints and subsequent joint damage, factor VIII infusions should be given regularly thrice a week starting from early childhood (around 2 years of age).
4. Synthetic vasopressin (desmopressin, an analogue of vasopressin) is given intravenous, subcutaneous or intranasally. It produces 3–5-fold rise in factor VIII:C and is very useful in patient with a baseline level of factor VIII >10 IU/dL. It prevents the complications associated with blood products. It is useful for treating bleeding episodes in mild haemophilia and as prophylaxis before minor surgery, ineffective in severe haemophilia. It is also given for vWD, but not in Christmas disease.

N.B. Remember the following points:

- 1 unit/kg factor VIII will raise blood level by 2%. So, the dose of factor VIII is calculated as follows:
- **FVIII dose = Desired factor VIII level – FVIII baseline level × Body weight (kg) × 0.5 unit/kg.**
- Previously, factor VIII was prepared from plasma. It is now prepared by recombinant DNA technology (so, there is less risk of transfusion transmitted infection, but more expensive).
- Advice to the patient—trauma should be avoided and precaution should be taken before tooth extraction and surgery. The patient should carry a special medical card in which details of the disease and its treatment must be recorded.
- Half-life of factor VIII:C is 12 hours.

Q: What are the **complications** of haemophilia?

A: As follows:

1. Due to repeated haemorrhage:
 - Arthropathy due to repeated bleeding in joint (e.g. knee, elbow).
 - Atrophy or wasting of muscles secondary to haematoma in muscle.

- Mononeuropathy due to pressure by haematoma.
- Death may occur due to intracerebral haemorrhage.

2. Due to therapy:
 - Infections: Hepatitis A, B, C, D. Also, HIV.
 - Factor VIII antibody (up to 30% patients with severe haemophilia).

N.B. Remember the following points:
- Risk of viral transmission is eliminated because of prior screening of donors.
- Infectious agents that can cause Creutzfeldt–Jakob disease may be transmitted by blood and blood products.
- All patients should receive vaccination for HAV and HBV.
- Use of recombinant factor VIII effectively eliminate transfusion transmitted infection.

Q: What are the **causes of death**?
A: As follows:
- Bleeding, mainly intracerebral.
- HIV related.
- Hepatitis due to HCV.

Q: If **factor VIII antibody** develops, how can it be suspected and treated?
A: It is suspected if no response to factor VIII in therapeutic dose. APTT is prolonged. In normal haemophilia, APTT is corrected by addition of normal plasma in 1:1 ratio. But if factor VIII antibody develops, APTT is not corrected with normal plasma in this ratio. This case is very difficult to treat. Following options are available:
- High dose and frequent infusion of factor VIII may be given.
- Changing the species such as porcine factor VIII may be used.
- Factor IX may be used. It helps bypassing the inhibitors.
- Recombinant factor VIIa helps bypassing the inhibitors.
- Factor eight inhibitor bypassing activity (FEIBA, an activated concentrate of factors II, IX and X), or, prothrombin complex concentrate (PCC), which contains factor VII, IX and X may be used.
- Sometimes, immunosuppressive therapy such as steroid, azathioprine or cytotoxic drugs may be given.
- In long term, management is to eradicate inhibitory antibody. This can be done by using immune tolerance induction (ITI). Recently, anti-CD20 monoclonal antibody (rituximab) as coadjuvant is promising.

Christmas Disease

It is also called haemophilia B. It is due to deficiency of factor IX. Features are like haemophilia A. It is treated with factor IX concentrate, half-life is 24 hours. Prophylaxis is given twice a week. Desmopressin is ineffective.

Reiter Syndrome

Usual instructions are:
- Examine the legs or knee joints.

Presentation of a case: (as in knee joint, the patient is young adult)

Q: What **history** do you like to take from the patient?
A: History of urethritis, diarrhoea or dysentery (*Shigella*, *Campylobacter* and *Yersinia*), and sexual exposure (*Chlamydia*).

Q: What **else** do you want to examine?
A: I want to examine:
- Eyes (conjunctivitis, usually bilateral, may be iritis in 10%).
- Back (evidence of sacroiliitis, SI).
- Foot (heel pain, Achilles tendinitis and plantar fasciitis).
- Circinate balanitis and keratoderma blennorrhagica (in palm, sole and toes).



Circinate balanitis (glans penis)



Circinate balanitis (involving skin)



Keratoderma blennorrhagica



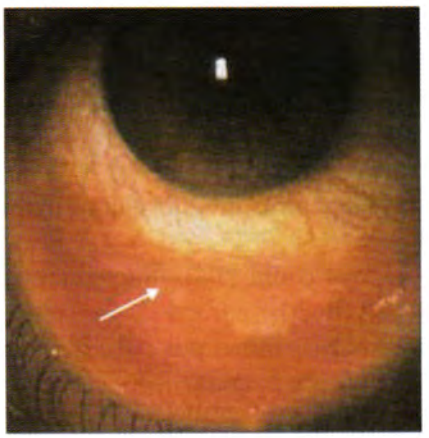
Keratoderma blennorrhagica (severe)



Keratoderma blennorrhagica (palm; a few blisters and thickening)



Keratoderma blennorrhagica (palm; more blisters)



Conjunctivitis

Q: What is the **triad** of Reiter syndrome?

A: Triad:

- Arthritis.
- Conjunctivitis.
- Urethritis (non-specific).

Reiter syndrome is common in males (M:F = 15:1), 16–35 years. Male with human leucocyte antigen (HLA) B27 has 20% risk of suffering the disease after *Shigella* dysentery.

Q: What is **Reiter syndrome** and **reactive arthritis**?

A: As follows:

- Reiter syndrome is a seronegative arthritis characterized by arthritis, conjunctivitis and urethritis.
- Reactive arthritis means when only arthritis follows after an attack of diarrhoea, and dysentery or sexual exposure (pathology in one site, but affecting the joints). It is actually a variety of Reiter syndrome. Organisms are *Salmonella*, *Shigella*, *Campylobacter*, *Chlamydia* and *Yersinia*.

Q: How does a patient with Reiter syndrome usually present?

A: As follows:

1. History of diarrhoea, dysentery or sexual exposure.
2. After 1–3 weeks, asymmetrical oligoarthritis involving the bigger joints (knee and ankle), conjunctivitis and urethritis.
3. Extra-articular features:
 - Conjunctivitis and iritis.
 - Achilles tendinitis and plantar fasciitis.
 - Circinate balanitis.
 - Skin rash (macular, vesicular or pustular).
 - Keratoderma blennorrhagica (in palm, sole or toes).
 - Nail dystrophy and buccal erosion.
 - Others (rare) include pericarditis, aortic regurgitation, conduction defect, pleurisy, peripheral neuropathy and meningoencephalitis.

Q: What **investigations** should be done in this patient?

A: As follows:

- Hb%, total count (TC), differential count (DC) and ESR (high).
- Urine analysis shows pus cells, sterile on routine culture (sterile pyuria).
- CRP (high).
- RA test and ANF (negative).
- X-ray of the joints involved and SI joint (ankylosing spondylitis).
- If joint effusion is present, aspiration of fluid and analysis (complement is high in synovial fluid).
- HLA-B27 positive in 70% of the cases (in affected persons).

Q: What is **keratoderma blennorrhagica**?

A: Skin lesion characterized by vesiculopapules with desquamated margin, which coalesces to form crusty plaques. Usually found in palm and sole, also scrotum, scalp and trunk. It may disappear and recur also. Nail dystrophy and subungual hyperkeratosis may occur. It is confused with pustular psoriasis. Treated with methotrexate or azathioprine.

Q: How to **treat** Reiter syndrome?

A: As follows:

- Rest and NSAID for pain. Sometimes, local steroid injection.
- Antibiotic (tetracycline and erythromycin for non-gonococcal urethritis).
- Usually, single attack, which settles.
- In some cases of recurrent and remitting arthritis, disease-modifying drugs, such as sulphasalazine or methotrexate or azathioprine, should be given.
- In severe cases, steroid may be given.
- Anti-TNF therapy may be helpful in some severe cases.
- Physiotherapy.

Q: What are the **differences** between gonococcal arthritis and Reiter syndrome?

A: As follows:

Features	Gonococcal arthritis	Reiter syndrome
Involvement of joints	Mainly of upper and lower extremities	Mainly lower extremity
Vesicular lesion	Common	Uncommon
Backache (ankylosing spondylitis)	Unusual	Common
Organism	*Gonococcus* isolated from smear	No definite organism found

Psoriatic Arthropathy

Usual instructions are:

- Examine the lower limbs or knee joints.
- Examine the hands.

Presentation of a Case (Lower Limbs or Knee): Case No. 1

Present as in knee joint arthritis. Look for skin rash and nail changes.

Q: What **else** do you want to examine?

A: I want to examine the skin to see psoriatic patch and nail changes.

Presentation of Case (Hand): Case No. 2

- There is swelling with gross deformity of right (or left), second and third DIP joint and first PIP joint. There is also (may be) deformity of MCP (mention which one). Arthropathy is asymmetrical.
- In nails, pitting, thickening of nail plate, hyperkeratosis and onycholysis are seen.
- There is a small psoriatic patch at the dorsum of right (or left) hand.

My diagnosis is **psoriatic arthritis**.



Psoriatic arthritis with psoriatic patch



Typical skin lesion in psoriasis



Nails pitting



Nails in psoriasis



Psoriatic arthritis (DIP) with patch and nail lesion



Psoriatic arthritis (DIP and MCP)

Q: What are the sites of **psoriatic patch**?

A: Wrist, elbow, scalp, hairline, back of ear, natal cleft, around umbilicus, shin, knee and extensor surfaces of limbs and scrotal region.

Q: What are the **other possibilities**?

A: As follows:

- Gout.
- Osteoarthrosis.

Q: Why **not** this is a case of RA?

A: Because in RA:

- PIP joints are involved. No involvement of DIP.
- Arthritis: bilateral and symmetrical.
- Skin lesion and nail changes are absent in RA.

Q: What are the **types of arthritis** in psoriasis?

A: There are five types:

- Asymmetrical inflammatory oligoarthritis (of hands and foot): 40%.
- Symmetrical seronegative polyarthritis (like rheumatoid): 25% (no rheumatoid nodule and involvement of PIP, DIP, MCP joints, and nail changes help to diagnose; 50% of the cases develop arthritis mutilans).

- SI or spondylitis: 15%. More in males, psoriatic lesion before arthritis, and nail changes are usually present.
- Predominant DIP joint arthritis: 15% (typical), nail dystrophy is invariable.
- Arthritis mutilans: 5%.

Q: What are the **nail changes** in psoriasis?

A: Nail change is present in 85% of the cases of psoriasis:
- Nail pitting.
- Onycholysis.
- Subungual hyperkeratosis.
- Horizontal ridging and thickening of nail.

Q: What are the other diseases causing **nail change**?

A: As follows:
- Fungal infection.
- Reiter syndrome.

Q: What are the diseases affecting **DIP joint**?

A: As follows:
- Psoriasis.
- Gout.
- Osteoarthrosis.

Q: What are the causes of **arthritis mutilans**?

A: As follows:
1. Rheumatoid arthritis.
2. Psoriatic arthritis.
3. Juvenile idiopathic arthritis.

Q: What **investigations** do you suggest in psoriatic arthritis?

A: Diagnosis is clinical. For exclusion of other diseases, following tests are done:
1. CBC (ESR may be high).
2. CRP (high).
3. RA and ANF (negative).
4. Radiology: X-ray of the joint involved (hand, foot and SI joint) may be normal:
 - X-ray of the hand shows destruction of DIP joint with deformity, punched out lytic lesion, pencil-in-cup appearance (narrow distal end of the proximal bone fits into the splayed out proximal end of the distal bone) and extensive bone resorption resulting in "**opera glass hand**" (one bone enters into its neighbouring bone like a telescope, thus giving rise to this appearance).
 - X-ray of the SI joint (ankylosing spondylitis).
 - Serum uric acid (may be high) can cause secondary gout.



X-ray in psoriatic arthritis (DIP)
(arthritis of DIP in fourth and fifth finger)



X-ray in psoriatic arthritis (DIP)
(severe polyarthritis of DIP and PIP)

Q: How to **treat** psoriatic arthritis?

A: As follows:
1. Treatment of psoriasis: General measures, local therapy and systemic therapy (for details see chapter on Dermatology).
2. Treatment of arthritis:
 - NSAID (however, some NSAIDs may aggravate psoriasis).
 - In persistent and progressive: Sulphasalazine and methotrexate or azathioprine (these drugs will help in both skin lesion and arthritis). Cyclosporine may be used.
 - Biological agents: Monoclonal antibody that produces dramatic response in psoriasis (e.g., infliximab, etanercept or adalimumab may be given when all other drugs fail. Rituximab has no role in psoriatic arthritis).
 - In retinoid, acitretin 20 mg daily is effective in both arthritis and skin lesion (avoid in young female as it is teratogenic).
 - Prednisolone may be needed (sometimes steroid is given intra-articularly).
 - PUVA is mainly for skin lesion. Sometimes helpful in arthritis when synchronous skin lesion and arthritis are present.

N.B. Remember the following points:

- 7% of psoriasis patients develop arthritis.
- Arthritis occurs in 20% cases before the onset of psoriasis. Arthritis is present with current or previous psoriasis in 70% cases. In 5% cases, synchronous onset of skin lesion and arthritis.
- No skin lesion in 5% cases.
- Age: Third or fourth decade (25–40 years).
- Equally present both in males and females (but ankylosing spondylitis is twice more in males than in females).
- 50% of the patients with ankylosing spondylitis are HLA-B27 positive.
- Spontaneous remission of arthritis may occur.
- Avoid the following drugs (which may aggravate psoriatic skin lesion, the exfoliative lesion): Chloroquine and hydroxychloroquine, lithium, beta-blocker, ACE inhibitor and alcohol.

Q: Name some drugs that are effective both in psoriasis and arthritis.

A: Methotrexate, sulphasalazine, cyclosporine, azathioprine and biological agents.

Q: What are the common complications of anti-TNF-alpha therapy?

A: As follows:

- Flare of tuberculosis.
- Haematological malignancy.
- Worsening of heart failure.
- Blood dyscrasia—anaemia, thrombocytopaenia, leucopaenia, aplastic anaemia.

Q: What are the contraindications of anti–TNF-alpha therapy?

A: As follows:

- Active tuberculosis (2 months anti-TB therapy should be given before starting anti–TNF-alpha therapy)
- Latent tuberculosis.
- Active bacterial infection.
- CCF.
- Septic arthritis in previous 1 year.
- Demyelinating disease.
- Pregnancy and breast feeding.

Ankylosing Spondylitis

The usual instructions are:

- Examine the back and relevant parts.
- Look at the patient and examine (patient may be standing or lying).

Proceed as follows (patient should be examined in lying and in standing position):

During lying:

- See SLR (ask the patient to raise the straight leg. The patient may complain of pain on the affected side, which indicates root pressure due to disc prolapse.)
- Abdomen (appears protruded).
- Examine for evidence of sacroiliitis (compressing iliac bones).
- Assess the movement of hip joint.
- See the chest expansion, and examine lungs for apical fibrosis.
- Examine heart for aortic regurgitation (AR).
- Examine the eyes (for iritis).
- Examine the foot for Achilles tendinitis and plantar fasciitis.

Now, ask the patient to stand up and perform the following points:

- Observe whether there is fixed thoracic kyphosis, loss of lumbar lordosis and compensatory hyperextension of neck.
- Ask the patient to look up (patient is unable to do).
- Ask the patient to turn either side (whole body turns when the patient attempts).
- Ask the patient to stand along the side of wall with the back (inability to make contact of the body against the wall).
- See the range of movement of spine by flexion, extension and lateral bending of body (see any restriction).
- Perform Schober test as follows:
 - Mark two points 10 cm above and 5 cm below a line joining the dimple of Venus on the sacral promontory (the line passes along L_5, and dimple indicates the site of posterior superior iliac spine).
 - Ask the patient to bend forward as far as possible.
 - Now measure the distance between upper and lower markings.

Normally, it increases by >5 cm below 50 years of age. If <5 cm, it indicates limitation of mobility of spine.

Modified Schober test: Only the upper marking is taken, which is sufficient for the test, as the lower part is remaining fixed. It is called modified Schober test.

Q: Ask some **questions** to the patient?

A: Low back pain with morning stiffness, any skin lesion (psoriatic arthritis) and history of frequent loose motion or bloody diarrhoea (inflammatory bowel disease).

Presentation of a Case

- There is loss of lumbar lordosis, thoracic kyphosis and compensatory hyperextension of neck (in advanced stage, **question mark "?"** or stooped posture).
- The patient is unable to look up and unable to turn to any side without movement of whole body.
- There is restricted movement of spine in all directions (forward, lateral and backward bending).
- SLR is positive.
- The patient is unable to make contact between the occiput and the wall when standing with heel and back against the wall (ask the patient to stand along the side of the wall with heel and back against the wall, now measure occiput to wall distance. Gap indicates limitation of thoracic and cervical spine).
- Sacroiliitis is present.
- Achilles tendinitis and plantar fasciitis are present.
- Right knee joint is mildly tender and swollen with slight reduction of movement.
- Schober test is positive.
- Abdomen is protruded.

My diagnosis is **ankylosing spondylitis**.



Juvenile ankylosing spondylitis



Protruded abdomen, thoracic kyphosis, lumbar lordosis

Q: What are your **differential** diagnoses?

A: Any cause of spondyloarthropathy may be considered as differential diagnosis.

- Reiter syndrome or reactive arthritis.
- Enteropathic arthritis (Crohn disease and ulcerative colitis).
- Psoriatic arthritis.
- Juvenile chronic arthritis (if the patient is <16 years old).

Q: What **else** do you want to see in ankylosing spondylitis?

A: I want to see extra-articular features:

- Eye (to see iritis).
- Heart (AR).
- Chest and lungs (restricted movement of chest, apical fibrosis, pulmonary hypertension and cor pulmonale).
- Foot (Achilles tendinitis and plantar fasciitis).

Q: What are the other **causes** of sacroiliitis?

A: Any cause of spondyloarthropathy.

Q: How to **differentiate** AR of rheumatic heart disease and of ankylosing spondylitis?

A: From **history** and **echocardiogram**:

- In rheumatic heart disease, echocardiogram shows the involvement of valve cusps (shortening, thickening and fusion).
- In ankylosing spondylitis, echocardiogram shows involvement of aorta or aortic root dilatation due to aortitis.

Q: What is **spondyloarthropathy** or **spondarthritis**?

A: It is a group of inflammatory arthritis characterized by:

1. Seronegative rheumatoid factor (RA test is negative).
2. Sacroiliitis and inflammatory spondylitis.
3. Asymmetrical inflammatory oligoarthritis (lower > upper limbs, bigger joints are involved).
4. Inflammatory enthesitis.
5. Absence of nodules and other extra-articular features of rheumatoid arthritis.
6. Typical overlapping extra-articular features:
 - Mucosal inflammation (such as conjunctivitis, buccal ulceration, urethritis, prostatitis, bowel ulceration).
 - Pustular skin lesions and nail dystrophy.
 - Anterior uveitis.
 - Aortic root fibrosis (AR, conduction defects).
 - Erythema nodosum.
7. Familial association (high in HLA-B27).

Q: What are the **diseases** in spondyloarthropathy?
A: As follows:
- Ankylosing spondylitis.
- Reiter syndrome or reactive arthritis.
- Enteropathic arthritis (Crohn disease and ulcerative colitis).
- Psoriatic arthritis.

Q: What are the **types** of ankylosing spondylitis?
A: There are two types:
- Primary: Without any other association.
- Secondary: When associated with other seronegative arthritis.

Q: What is **enthesopathy**?
A: Inflammation at the ligamentous attachment with erosion of adjacent bone. Healing of such lesion at the junction of intervertebral disc and vertebral bodies causes new bone formation, called syndesmophyte (**hallmark** of ankylosing spondylitis).

Q: What is **ankylosing spondylitis**? What are the usual **presentations**?
A: It is a chronic inflammatory seronegative spondarthritis characterized by progressive stiffening and fusion of axial skeleton. Age is second and third decade, M:F = 3:1.

The patient usually presents with low back pain with morning stiffness, worse in the morning and with inactivity, and pain improves after exercise. Peripheral arthritis occurs in 10% cases.

Q: Is there any **peripheral arthritis** in ankylosing spondylitis?
A: May occur in juvenile onset disease, also in 20–30% of adult cases. Hip and knee are commonly affected.

Q: What is the cause of **chest pain** in ankylosing spondylitis?
A: Chest pain is due to costochondral junction involvement.

Q: What is the **nature of arthritis** in ankylosing spondylitis?
A: Inflammatory.

Q: What are the **extra-articular manifestations** of ankylosing spondylitis?
A: As follows:

1. Eyes: Uveitis (iritis) 25%, conjunctivitis 20% (the patient may present with painful red eye and photophobia).
2. Heart:
 - AR (4%, due to aortitis), mitral regurgitation.
 - Conduction defect (first-degree block, left bundle branch block [LBBB]), and atrioventricular block (AV block), and pericarditis.
3. Chest and lungs:
 - Chest pain (pleuritic) and reduced chest expansion (costovertebral joint involvement). Apical pulmonary fibrosis, cavitation and later on aspergilloma may occur.
 - Pulmonary hypertension and cor pulmonale.
4. Prostatitis (80%), usually asymptomatic.
5. Neurological: Cauda equina syndrome (there is weakness of lower limb, loss of sphincter and rectal control and saddle sensory loss).
6. Others include plantar fasciitis, Achilles tendinitis, amyloidosis and osteoporosis.

Q: What are the **diagnostic criteria** for AS?
A: The presence of 3 of following 4 in adults <50 years with chronic back pain indicates AS:
- Morning stiffness >30 minutes.
- Improvement of back pain with exercise but not rest.
- Awakening because of back pain during second half of the night only.
- Alternating buttock pain.

Alternately, Modified New York Criteria (1984) is used:
- Low back pain at least 3 months duration increased by exercise relieved by rest.
- Limitation of lumbar spine movement in at least 2 planes.
- Decreased chest expansion less than normal.
- Bilateral sacroiliitis grade 2–4.
- Unilateral sacroiliitis grade 3–4.

Definite AS: Sacroiliitis with any clinical criteria.

Q: What are the **investigations** done in ankylosing spondylitis?

A: As follows:

1. X-ray of SI joints and spine (lumbosacral, dorsal and cervical).
2. MRI of lumbosacral spine may be done in some cases (more sensitive than X-ray).
3. CBC (ESR may be high).
4. CRP (may be high).
5. Rheumatoid factor (negative).
6. HLA-B27 (measured in blood lymphocytes; is positive in 90% of the cases).
7. Others according to cause (barium enema and follow through for inflammatory bowel disease).

N.B. HLA-B27 is neither necessary nor sufficient for diagnosis of AS. However, presence of HLA-B27 increases the probability of AS. In typical AS with absence of HLA-B27, there is probability of IBD.

X-ray shows:

- Sacroiliitis: Often the first abnormality, beginning in the lower synovial parts of the joints with irregularity and loss of cortical margins, widening of the joint space and subsequently sclerosis, narrowing and fusion.
- In thoracolumbar spine: Squaring of vertebrae due to erosion. Bridging syndesmophytes formation at the outermost fibres of the annulus results in **bamboo spine appearance**. There may be ossification of anterior longitudinal ligament or interspinous ligament and facet joint fusion.

Radiographically, ankylosing spondylitis may be confused with alkaptonuria, DISH, lumbar spondylosis and osteitis condensans ilii. Features are as follows:

- In alkaptonuria, calcification looks like AS. But there is calcification of intervertebral disc in alkaptonuria, never in AS.
- DISH (Diffuse idiopathic skeletal hyperostosis): Florid new bone formation along the anterolateral aspects of at least four contiguous vertebral bodies. In DISH, calcification gives the appearance of **flowing wax** on the anterior body of vertebrae. Sacroiliac and apophyseal joints are normal in DISH. It occurs in middle aged and elderly, usually asymptomatic.
- In lumbar spondylosis, there is disc space narrowing and marginal sclerosis.
- In osteitis condensans ilii, there is sclerosis on the iliac site of sacroiliac joints, confuses with sacroiliitis. It is a postpartum radiographic finding.



X-ray shows calcification of longitudinal ligament and bamboo spine appearance



X-ray of lumbar spine shows syndesmophyte formation

Q: What are the **differences** between syndesmophyte and osteophyte?

A: As follows:

Syndesmophyte	Osteophyte
Secondary to inflammatory disease	Degenerative
It grows longitudinally (above or below) causing bridging of adjacent vertebra	It grows horizontally outwards
Due to endochondral calcification of annulus fibrosus	New bone at the corners of vertebra
Hallmark of ankylosing spondylitis	Hallmark of osteoarthrosis

Q: What is the **natural history** of ankylosing spondylitis?

A: Up to 40% may develop severe spinal restriction, 20% may have significant disability. Early peripheral joint disease, especially hip joint involvement indicates poor prognosis.

Q: How would you perform **genetic counselling** with this patient?

A: If the patient is HLA-B27 positive, there is 30% chance for the siblings to develop ankylosing spondylitis.

Q: How to **treat** ankylosing spondylitis?

A: As follows:

1. General measures:
 - Patient's counselling and education.
 - Exercise is the mainstay. The patient must remain active. Swimming is the best activity.
 - Prolong sitting or inactivity should be avoided.
 - Physiotherapy.
 - Occupational therapy.
2. Drug treatment:
 - NSAID to relieve pain.
 - DMARDs—sulphasalazine or methotrexate (MTX) are helpful in peripheral arthritis, but has no effect on axial disease.
 - In patient with persistent active inflammation, anti-TNF drug therapy (etanercept, adalimumab, infliximab) may be helpful for both spinal and peripheral arthritis.
 - Local steroid injection may be given for persistent plantar fasciitis, other enthesopathies and peripheral arthritis.
 - Oral steroid may be needed for acute uveitis.
 - Other drugs: Thalidomide, pamidronate (may be used in resistant cases).
3. Orthopaedic measures: May be needed for severe hip, knee or shoulder restriction.

Q: What is the **prognosis**?

A: With appropriate treatment, the prognosis is usually excellent and there is minimum disability unless the hip joints are involved. Around 80% patients remain fully employed.

N.B. Remember the following points:

- Disease is mild in women. Peripheral arthritis is more in women. Spinal arthritis is less.
- May be severe, when it affects in early age, also worse prognosis.
- Hip joint involvement is more in teen age.
- In the past, radiotherapy was given, which is not used nowadays, because there is 10-fold increased incidence of leukaemia (AML).

Dermatomyositis or Polymyositis

Usual instructions are:

- Look at the patient or face. What are your findings?
- Examine the hands and relevants of this patient.

In the **face**, see the following points:

- Skin rash (macular, maculopapular, scaly and erythematous) over the cheeks and forehead. There may be butterfly rash and erythema-resembling sunburn.
- Heliotrope rash around the eyelid (commonly in the upper eyelid).
- Periorbital oedema.
- Puffy face.
- Telangiectasia.
- Erythematous rash may be present on the neck and upper chest (in the shape of V – called V sign), or on the shoulders (Shawl sign).

In the **hands**, see the following points:

- Skin rash (macular, maculopapular, scaly and erythematous) on the dorsum of hands (usually spares the phalanges, unlike SLE that involves the phalanges, but spares the knuckles).
- Finger shows periungual erythema, dilated nailfold capillary (telangiectasia), ragged cuticles and haemorrhage.
- Gottron sign (see below).
- Joint changes (swelling, tenderness and contracture).

For **relevants**, see the following points:

- Skin rash in other parts of the body.
- Look for evidence of proximal myopathy (both in upper and lower limbs).
- Tenderness of muscles (present in 50% of the cases of polymyositis).

Presentation of Case No. 1 (Face)

- In the face, there is erythematous, maculopapular, scaly rash over the cheeks and forehead.
- There is heliotrope rash in upper eyelids of both eyes and periorbital oedema.

My diagnosis is **dermatomyositis**.

Q: What **else** do you like to see?

A: I want to see skin lesion in other parts of the body, proximal myopathy and joints. Also, I want to exclude other primary causes, especially malignancy (such as bronchial carcinoma).

Presentation of Case No. 2 (Hand)

- There are multiple maculopapular, scaly, erythematous rash on the dorsum of both hands. Also, rashes with flat topped macules over the knuckles (Gottron sign) are present.
- In the finger, there are periungual erythema, ragged cuticles, haemorrhage and telangiectasia (dilated nailfold capillary).
- Joints are swollen, tender with contracture deformity.

My diagnosis is **dermatomyositis**.



Face in dermatomyositis



Dermatomyositis

Q: What are the **differential diagnoses**?

A: As follows:

- Drug rash.
- Systemic lupus erythematosus (or discoid lupus erythematosus, DLE).
- Mixed connective tissue disease (MCTD).
- Systemic sclerosis.
- Sarcoidosis.
- Acne rosacea.
- Lepromatous leprosy.

Q: What is **polymyositis** or **dermatomyositis**?

A: Polymyositis is the non-suppurative, non-infective inflammation of skeletal muscle characterized by necrosis, fibrosis and regeneration of muscles. When associated with **skin rash**, it is called dermatomyositis.

Q: How do you **classify** dermatomyositis/polymyositis?

A: Five types:

1. Adult polymyositis.
2. Adult dermatomyositis.
3. Dermatomyositis or polymyositis associated with malignancies.
4. Childhood dermatomyositis or polymyositis.
5. Dermatomyositis or polymyositis associated with other autoimmune rheumatic disease (ARD, e.g. SLE, rheumatoid arthritis and SSc).

Q: What are the **causes** of dermatomyositis?

A: Actual cause unknown. Probable factors are:

- Autoimmune mechanism (presence of anti-Jo-1 antibody and lymphocyte infiltration in muscle).
- Viral (coxsackie B, rubella and influenza have been suggested).
- Associated with malignancy (commonest cause is bronchial carcinoma in male and ovarian carcinoma in female). Dermatomyositis can precede any malignancy of lungs, ovary, breast, stomach.
- Drugs causing polymyositis—penicillamine and zidovudine.

Q: If the patient is **elderly**, what disease should be excluded?

A: Malignancy (bronchial carcinoma, also carcinoma of the breast, GIT and ovary).

Q: What are the **presentations** of dermatomyositis?

A: Common in female, F:M = 2:1, peak incidence is in fifth and sixth decades.

- Muscular weakness, mainly involving the proximal muscles (shoulder and pelvic girdle).

- Skin rash—typically affects upper eye lids with erythema called "heliotrope rash" (photosensitive, erythematous and scaly). Flat, red rash on face and upper trunk, erythematous rash of knuckles with raised violaceous scaly eruption (Gottron sign). Erythematous rash also may occur in knee, elbow, malleoli, neck and anterior chest (often a V sign) or back and shoulder (shawl sign).
- Pharyngeal, laryngeal and respiratory muscles involvement may cause dysphagia, dysphonia and respiratory failure.
- Others: Arthralgia, arthritis, myalgia and Raynaud phenomenon.

N.B. Remember the following points:

- In some patients, only skin rash may be present without muscle involvement called **dermatomyositis sine myositis**.
- Ocular involvement is rare.
- Malignancy is more in dermatomyositis, less in polymyositis.
- The patient may present with acute renal failure due to myoglobinuria secondary to rhabdomyolysis.

Q: What is the **pathognomonic sign** in dermatomyositis?
A: Heliotrope rash.



Heliotrope rash

Q: What is **heliotrope rash**?
A: It is a violaceous, purple or lilac coloured rash, present usually over the eyelids. It may also be present on the cheeks, nasal bridge and knuckles.

Presence of heliotrope rash is highly suggestive of dermatomyositis. It is derived from the name of the shrub *Heliotropium*, which has fragmented, purple flowers. It is more common in childhood dermatomyositis, also occurs in adults.

Q: If the patient is **elderly**, what do you think is the underlying cause?
A: May be associated with neoplasm (commonly bronchial carcinoma, also carcinoma of the breast, GIT and ovary).

Q: What is **Gottron sign**?
A: It is scaly, purple-red, raised, flat-topped, and vasculitic patches over the extensor surface of joints and knuckles of hands. It may be found on the elbow and knee.

Q: What **other skin lesion** may resemble Gottron papule?
A: SLE, psoriasis, lichen planus.



Gottron sign

Types of dermatomyositis or polymyositis

There are five types:

- Primary idiopathic polymyositis.
- Primary idiopathic dermatomyositis.
- Dermatomyositis or polymyositis associated with neoplasia.
- Childhood dermatomyositis or polymyositis associated with vasculitis.
- Dermatomyositis or polymyositis associated with collagen vascular disease.

Q: What are the **presentations** of dermatomyositis?
A: Common in female, F:M = 3:1, and with age in fourth and fifth decade.

- Gradual and progressive muscular weakness and wasting, mainly involving the proximal muscles (shoulder and pelvic girdle).
- Skin rash (photosensitive, erythematous and scaly).
- Pharyngeal, laryngeal and respiratory muscles involvement may cause dysphagia, dysphonia and respiratory failure.
- Others include arthralgia, arthritis, myalgia, dysphagia and Raynaud phenomenon.



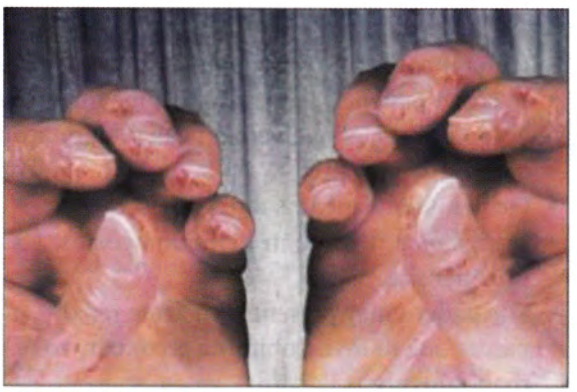
Skin rash in dermatomyositis



Heliotrope rash and butterfly rash



Skin rash in dermatomyositis (leg)



Dermatomyositis (contracture)



Skin rash in dermatomyositis (body)



Skin rash in dermatomyositis (hands)

Q: What **investigations** should be done in dermatomyositis?

A: As follows:

1. FBC (ESR is high, but may be normal even in active disease).
2. Muscle enzymes:
 - Creatine phosphokinase (CPK) is very high (the most sensitive test).
 - Other enzymes—serum aldolase, SGOT, SGPT and LDH (may be high).
3. Electromyography—abnormal almost in every case, normal in 10%.
4. Muscle biopsy shows the following findings:
 - Necrosis, swelling, vacuolation, disruption and fragmentation of muscles.
 - Infiltration of lymphocyte, plasma cells, eosinophils and macrophages.
 - Fibrosis.
 - Perivascular inflammatory cells infiltration and thickening of vessel wall.
5. Other tests:
 - To exclude malignancy (chest x-ray, USG, CT scan, MRI, PET scan, mammogram, gastrointestinal tract imaging).

- Other x-rays (limbs or hands) to see soft tissue calcification. It is common in childhood dermatomyositis.
- RA test and ANF (positive in 50% cases).
- Anti-Jo-1 antibody is more specific. Positive in 30% cases of dermatomyositis and 50% cases of polymyositis (if anti-Jo-1 antibody is present, respiratory muscles involvement may occur).
- MRI of muscles, to detect abnormal muscles (helpful to take biopsy).
- Urine for myoglobin in acute cases.

Measurement of CPK is important for the following reasons:

- Very high in dermatomyositis.
- Indicates active disease.
- To see therapeutic response (reduces after therapy).

Occasionally, CPK may be **normal** in dermatomyositis:

- If dermatomyositis is associated with internal malignancy.
- Due to long-standing disease with atrophy of muscles.
- Due to the presence of inhibitors in blood.

Q: What are the causes of high CPK?

A: As follows:

- Exercise.
- Intramuscular injection.
- Muscle trauma or road traffic accident.
- Convulsion.
- Alcoholism.
- Dermatomyositis or polymyositis.
- Acute myocardial infarction (CPK-MB).
- Myopathy.
- Rhabdomyolysis.
- Chronic liver disease (CLD).
- Drugs—statins, busulfan, narcotics, colchicine and chloroquine.

Iso-enzymes of CPK:

- MM (mainly in skeletal muscle).
- MB (mainly in cardiac muscle).
- BB (in brain).

Q: What are the **EMG findings** in dermatomyositis?

A: As follows:

- Spontaneous fibrillation (at rest).
- Small amplitude, short duration and polyphasic action potential (after voluntary activity).
- Salvos of repetitive potential on mechanical stimulation of the nerve.



Childhood dermatomyositis



X-ray showing calcification in dermatomyositis

Diagnostic criteria of dermatomyositis

There are four criteria:

- Typical clinical history.
- Increased muscle enzyme (CPK).
- EMG findings.
- Muscle biopsy.
- In a typical case with skin lesion, muscle biopsy is not essential. But in idiopathic polymyositis, muscle biopsy is necessary.

Q: How to **treat** dermatomyositis or polymyositis?

A: As follows:

1. General measures:
 - Patient education.
 - Physiotherapy.
 - Bed rest in severe case.
 - Avoidance of sunlight, use of sunscreen.

2. Medicine:
 - Prednisolone 0.5–1 mg/kg daily to induce remission. Continued for at least 1 month after myositis is clinically and enzymatically inactive. Then taper the dose slowly. Maintenance dose is 5–7.5 mg daily. May be required for months, even years.
 - If severe respiratory or pharyngeal weakness—Methylprednisolone 1 g daily for 3 days.
 - If no response to steroid—methotrexate or azathioprine may be given.
 - If methotrexate and azathioprine fail—cyclosporine or cyclophosphamide or mycophenolate mofetil may be tried.
 - High-dose IV immunoglobulin may help in refractory cases.
 - Rituximab may be used if all fail.
3. Treatment of underlying malignancy may improve the condition.

Q: What is the **prognosis**?

A: As follows:
- 5-year survival rate in treated patient is >95%; 10-year survival is 84%.
- Worse prognosis if severe in presentation, delay of treatment, severe dysphagia or respiratory difficulty, older patient and if underlying malignancy.
- Dermatomyositis responds better than polymyositis. So better prognosis.

Proximal Myopathy

Usual instructions are:
- Test for proximal myopathy.
- Examine the lower limb or upper limb.

Proceed as follows:
1. In the upper limb:
 - Ask the patient to raise the arms above head (patient is unable to do so).
 - Ask the patient to sit, abduct the arm (patient is unable), outstretch the arm in front (patient is unable), keep the arm on side at 90° and press against resistance.
2. In the lower limb:
 - While the patient is lying flat, ask him to raise the lower limbs (patient may be unable to do so).
 - Press the knee and ask the patient to raise the limbs against resistance.
 - Ask the patient to sit on the floor in squatting position. Then ask him to stand up (patient is unable to do so).
 - Ask the patient to walk (see the gait).



Proximal myopathy (wasting shown, severe)



Proximal myopathy (wasting shown, early stage)

Presentation of a Case

- There is proximal myopathy involving both the upper and lower limbs.

My diagnosis is **proximal myopathy**.

Q: Ask some **questions** to the patient (or what are the **complaints** by the patient)?

A: The patient may complain of difficulty in combing, climbing up stairs and rising from the chair (or ask the patient about these).

Q: What are the **causes** of proximal myopathy?

A: As follows:

- Dermatomyositis or polymyositis.
- Myasthenia gravis.
- Myasthenic myopathic syndrome (Eaton–Lambert syndrome).
- Myopathy (limb girdle, fascioscapulo humeral and mitochondrial), except myotonic dystrophy.
- Cushing syndrome.
- Diabetic amyotrophy.
- Thyrotoxicosis (also hypothyroidism).
- Polymyalgia rheumatica.
- Osteomalacia.
- Hyperparathyroidism.
- Periodic paralysis.
- Alcohol and drugs (steroid, chloroquine, amiodarone, lithium and zidovudine).
- McArdle syndrome (myophosphorylase deficiency, there is stiffness and cramps of muscle after exercise, which is hard and painful on movement).

Q: What are the **causes of painful muscle**?

A: As follows:

- Physiological (after exercise).
- Polymyositis or dermatomyositis.
- Polymyalgia rheumatica.
- Fibromyalgia syndrome.
- Viral infection.
- Chronic alcoholism
- Following convulsion
- Associated with rheumatological disease.
- Functional.

Q: What are the **causes of acute** or **sudden muscular weakness**?

A: As follows:

- Guillain–Barré syndrome.
- Hypokalaemia and hyperkalaemia.
- Familial periodic paralysis.
- Thyrotoxic periodic paralysis.
- Functional (hysterical conversion reaction [HCR]).

Q: What are the **drugs** causing myopathy?

A: Steroid, penicillamine, hydroxychloroquine or chloroquine, statins (lovastatin), zidovudine and clofibrate.

Q: What is **Eaton–Lambert syndrome**?

A: It is a paraneoplastic syndrome characterized by proximal muscle weakness and wasting due to defective acetylcholine release at the neuromuscular junction. It commonly involves the lower limb, but may involve any muscle.

Cause:

- There is defect in **acetylcholine** release at the neuromuscular junction, which is thought to be due to an auto-antibody against prejunctional voltage gated calcium channel on the motor nerve terminal. Small cell carcinoma of the lung may trigger the auto-antibody reaction.
- It is commonly due to small cell carcinoma of the lung, may be associated with or may precede the manifestations of carcinoma.

Features:

- Proximal weakness, commonly in the lower limbs but any muscle can be involved. Ptosis and diplopia may occur in 70% cases.
- Reflexes are absent or diminished.
- Muscle power may be increased and tendon reflexes may return after repeated activity or sustained contraction of the relevant muscle (reverse of myasthenia gravis).
- Patients may have autonomic dysfunction (dry mouth, constipation, impotence).

N.B. Abnormality of reflex, muscle power and autonomic disturbance are absent in myasthenia gravis.

Investigations:

- EMG shows progressive incremental response (reverse of myasthenia gravis where there is decremental response).
- Antibody to P/Q type voltage gated calcium channel (anti-VGLC)—found in 90% cases.

Treatment:

- 3, 4 diaminopyridine may be given.
- IV immunoglobulin may be helpful.
- Pyridostigmine may give symptomatic relief.
- Plasmapheresis.
- Treatment of the primary cause.

Gout

Usual instructions are:

- Examine the hands or foot.
- Look here (examiner may point a site). What is it? (Tophus.)

Look at the following points carefully (in the hands):

- Any deformity of the joints or swelling (symmetrical or asymmetrical).
- Presence of tophi (with skin necrosis, chalky or pasty material).
- Look for tophi in other parts (helix of ear, extensor and ulnar surface of the forearm, olecranon bursa, dorsum of hands and fingers, and Achilles tendon).

Presentation of a Case (in Hands)

- The patient has deformity with swelling of DIP joints, involving the fingers of right (or left) hand and also other small joints (mention which one).
- There is a tophus with necrosis over it with whitish or chalky discharge. Diagnosis is **gout** (if tophus is present, diagnosis is **chronic tophaceous gout**).

My diagnosis is **gout**.



Tophi in hands



Gout affecting elbow



Acute gout



Podagra



Chronic tophaceous gout



Tophus (confuses with Heberden node)



Tophus (helix of ear)

Q: What **relevant findings** do you want to see in gout?

A: As follows:

- Liver and spleen (lymphoma, myeloproliferative and lymphoproliferative disease).
- Lymph nodes (lymphoma).
- Evidence of psoriasis (skin lesion and nail change).
- Evidence of chronic renal failure (CRF and hypothyroidism).
- History of hypertension, DM, ischaemic heart disease (IHD) and drugs (see below).

Q: Which **joints** are involved in gout?

A: As follows:

- MTP (metatarsophalangeal) joint of the great toe >50% of the cases (called podagra).
- Other joints are ankle, midfoot, knee, small joints of hand, wrist and elbow.

Q: What are the **differential diagnoses** of gout?

A: The differential diagnoses of **acute gout** are:

- Traumatic.
- Septic arthritis.
- Pseudogout.
- Psoriatic arthritis.
- Reiter syndrome.

The differential diagnoses of **chronic gout** are:

- Pseudogout.
- Osteoarthrosis.
- Psoriatic arthritis.
- RA.
- Tuberculous arthritis.

Q: What is **gout**? What are the **types**?

A: Gout is a disorder of purine metabolism characterized by hyperuricaemia associated with the deposition of monosodium urate monohydrate (MSUM) crystals giving rise to arthritis, tenosynovitis, bursitis and tophaceous deposit. It is of two types:

- Primary: common in males, above 40 years.
- Secondary: common in females, above 65 years.

Q: What is **pseudogout**?

A: It is a crystal arthropathy caused by deposition of calcium pyrophosphate dihydrate (CPPD). It is also called chondrocalcinosis. Examination of synovial fluid under polarized light shows rhomboid shaped and positively birefringence CPPD crystals.

Q: What is **tophus**?

A: Nodular, hard and irregular swelling due to the deposition of urate with inflammatory cells surrounding them (tophus means chalk stone). It indicates chronic gout. Patients with severe tophaceous disease appear to have milder or less-frequent acute attack than non-tophaceous patients.

Tophus may have area of necrotic or ulcerated skin over it and may exude chalky material containing monosodium urate crystal. Tophus resolves slowly by treatment of hyperuricaemia.

Tophus confuses with:

- Rheumatoid nodule.
- Tendon xanthoma.
- Neurofibroma.
- Lipoma.

Causes of hyperuricaemia and gout:

1. Defect in renal excretion:
 - Renal failure.
 - Drugs include diuretic (thiazides), low-dose aspirin, pyrazinamide, ethambutol, nicotinic acid, ethanol, cytotoxic drug and cyclosporine.
 - Hyperparathyroidism.
 - Myxoedema.
 - Chronic lead poisoning.
 - Down syndrome.
 - Lactic acidosis (alcohol, starvation, toxaemia of pregnancy and type I glycogen storage disease).
2. Excess production of uric acid:
 - Myeloproliferative disease.
 - Lymphoproliferative disease.
 - Psoriasis.
 - Excess purine synthesis (hypoxanthine-guanine phosphoribosyltransferase [HGPT] deficiency, glucose-6-phosphatase deficiency).
 - Idiopathic (common)

Q: Could uric acid be **normal** in acute gout?

A: Yes, hyperuricaemia is common but not invariable. Usually, 5% of the hyperuricaemic patients develop gout.

Q: What are the **precipitating factors** of acute gout?

A: Acute attack may be precipitated by:

- Sudden rise of uric acid: Dietary excess or severe dietary restriction, alcohol and diuretic (thiazide).
- Sudden fall of uric acid by allopurinol or uricosuric drug.
- Others: Trauma, surgery and severe exercise.

Q: How does the patient usually **present with acute gout**? How to **investigate**?

A: In typical acute attack:

- Severe excruciating pain, mainly in metatarsophalangeal (MTP) joint of great toe, usually in early morning or late night, awaking the patient from sleep. Other joints are also involved.
- The joint is red, swollen and tender.

Q: What **investigations** should be done in gout?

A: Diagnosis is clinical.

- CBC: ESR (high), and leukaemia should be excluded.
- Serum uric acid.
- CRP (high).
- To be confirmed—aspiration from joint, bursa or tophus to see MSUM crystals under polarized microscope. It looks needle shaped and negatively birefringence crystals (but in pseudogout, calcium pyrophosphate dihydrate [CPPD] crystals are rhomboid and positively birefringence). It is intracellular (in leucocytes) in acute cases, may be extracellular.
- Other investigations—urea and creatinine (to exclude CRF), blood sugar, lipid profile, thyroid screening (to exclude hypothyroidism).

Q: What is the role of **serum uric acid level** to diagnose acute gout?

A: It has little value as in acute gout, serum uric acid may be normal. Asymptomatic hyperuricaemia is more common.

Q: How to **treat** acute gout?

A: As follows:

1. For pain: NSAID (indomethacin, naproxen and diclofenac oral or suppository).
2. If no response, colchicine 1 mg loading dose, then 0.5 mg every 6 hours till relief of symptoms. (Side effects include nausea, vomiting, diarrhoea and abdominal pain.)
3. In severe arthritis with effusion, aspiration and intra-articular steroid (methylprednisolone) may be given.
4. Long-term treatment:
 - Dietary restriction: Avoid uric acid containing diet (liver, kidney, brain, red meat, cabbage, cauliflower, carrot and spinach). Severe calorie restriction should be avoided. However, no need of strict specific dietary restriction.
 - Avoid alcohol and starvation.
 - Reduction of weight in obese patients (slow reduction).
 - Avoid precipitating drugs.
 - Allopurinol or other hypouricaemic drugs.
 - Febuxostat, a non-purine analogue inhibitor of xanthine oxydase.
 - Hypouricaemic drugs should not be given in acute attack, may be started after several weeks of acute attack.

Indications of hypouricaemic drug therapy:

- Recurrent attack of gout.
- Presence of tophi.
- Radiological evidence of joint damage.

Uricosuric drugs: Probenecid, sulphinpyrazone (high-dose aspirin and indomethacin may be uricosuric). Uricosuric drugs may be helpful if:

- No renal failure.
- Creatinine clearance >80 ml/min (if, <80 ml/min, less effective; if, <30 ml/min, it has no effect).
- Urine uric acid <700 mg/day on general diet.

Uricosuric drugs are **contraindicated** in:

- Gout with overproduction of uric acid and gross uricosuria.
- Renal failure.
- Urate lithiasis.

Brief Note on Allopurinol

Drug of choice. It inhibits the production of uric acid by inhibiting xanthine oxidase, responsible for conversion of xanthine and hypoxanthine to uric acid. Dose is 100–300 mg/day. In renal failure or old age, start with low dose (100 mg). Allopurinol should not be given in acute attack and is usually given several weeks after the acute attack. If given, it may precipitate acute attack. To prevent, NSAID or colchicine (0.5 mg 12 hourly) should be used together.

After allopurinol, uric acid should come down to half of the normal stage. Dose should be gradually increased, until this value is achieved. Drug should be continued indefinitely.

Q: What is **uric acid nephropathy**?

A: It means renal impairment is secondary to hyperuricaemia. There may be chronic renal failure, acute renal failure (due to obstructive uropathy) and nephrolithiasis. Nephropathy is due to:

- Urate deposition in renal parenchyma.
- Renal tubular obstruction and uric acid stone formation.

Asymptomatic Hyperuricaemia

1. It is 10 times more common.
2. No treatment is required in majority of the cases.
3. A search should be made to find out the secondary cause of hyperuricaemia.
4. Reduction of weight, avoidance of uric acid containing diet, alcohol and smoking.
5. Indication of treatment in asymptomatic hyperuricaemia:
 - If it is symptomatic.
 - 24 hours urine uric acid >1,100 mg/day.
 - Strong family history of gout, urate stone or renal failure or persistent high uric acid >10.1 mg.

Systemic Lupus Erythematosus (SLE)

Usual instructions are:

- Look at the face. What are your findings? What else do you want to see?
- Perform the general examination of the patient.

Presentation of a Case

- There are erythematous and scaly rash along the butterfly distribution and also in forehead.
- Some areas of scarring or depigmentation and telangiectasia are present.
- Face looks puffy and plethoric (due to steroid).

My diagnosis is SLE.



Discoid lupus erythematosus



Butterfly rash in SLE

Q: What **else** do you want to see?

A: I want to see the following features:

1. Skin rash in the other parts of body.
2. Mouth ulcer (sharply defined white patch with red margin).
3. Alopecia (non-scarring).
4. Arthropathy or arthritis.

Q: What **history** do you like to take in SLE?

A: I want to take the history of:

- Whether the rash is aggravated on exposure to sunlight.
- Drugs (see below) and oral pill.
- Repeated abortions in female.
- Convulsion, depression and unconsciousness or paralysis or paresis.
- Raynaud phenomenon (present in 20% of the cases).
- History of DVT or thromboembolism.
- Family history of SLE.

Q: What are your **differential diagnoses**?

A: As follows:

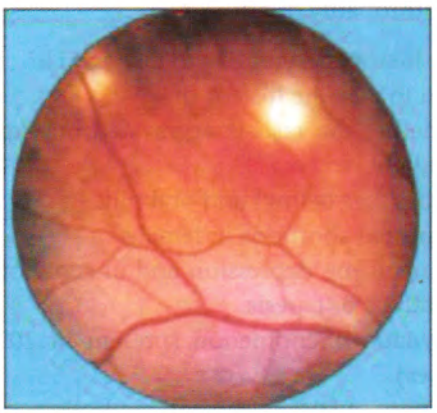
- SLE (or DLE).
- Dermatomyositis.
- Mixed connective tissue disease.
- Systemic sclerosis.
- Sarcoidosis.
- Drug rash.



Mouth ulcer in SLE (multiple)



Mouth ulcer in SLE



Cytoid body in SLE



Alopecia



Skin rash (SLE)



Arthritis of hand (SLE)

Q: What is SLE?

A: It is an autoimmune chronic multisystem disease characterized by production of multiple autoantibodies, immune complexes and widespread immune-mediated organ damage.

Q: From where is the **name** SLE derived?

A: Lupus means wolf. SLE is named because of the erosive nature of the condition that looks like the damage caused by hungry wolf's bite.

Q: What are the **manifestations** of SLE?

A: SLE is more in females, F:M = 9:1; age—in second and third decades. Sex ratio is equal in children and the elderly. It involves any organ of the body.

1. General features:
 - Fever.
 - Arthralgia, arthritis (non-erosive), myalgia.
 - Fatigue, tiredness, weakness, malaise.
 - Weight loss.
 - Skin manifestation (80%)—malar rash, discoid rash, photosensitivity, ulcer, vasculitic lesions on the finger tips and around the nail folds, livedo reticularis. (In discoid lupus, only skin is involved).
 - Scarring alopecia. Lupus hair (short broken hair above the forehead).
2. Heart (involved in 25%):
 - Pericarditis, pericardial effusion and myocarditis.
 - Rarely, non-infective endocarditis called Libman–Sacks endocarditis (common in anti-phospholipid syndrome). Mitral regurgitation may occur.
 - There is increased frequency of IHD and stroke in patients with SLE.
3. Vascular: Raynaud phenomenon, vasculitis, arterial and venous thrombosis (in anti-phospholipid syndrome) and atherosclerosis.
4. Lungs (involved in up to 50% cases):
 - Pleurisy, pleural effusion (may be bilateral) and pneumonitis.
 - Atelectasis and shrinking lung with elevation of diaphragm (shrinking lung syndrome).
 - Pulmonary fibrosis (rare, found in overlap syndrome).
 - Increased risk of thromboembolism.
 - Intrapulmonary haemorrhage with vasculitis (rare but dangerous).
5. Eyes:
 - Episcleritis, scleritis, conjunctivitis and optic neuritis (blindness is uncommon).
 - Secondary Sjögren syndrome (dry eye and dry mouth) in 15% cases.
 - Retinal vasculitis can cause infarct (fundoscopy shows white, hard exudate called cytoid body).
6. GIT (rarely involved):
 - Mouth ulcer (usually painless, but may be painful if secondary infection).
 - Mesenteric vasculitis (causing small bowel infarction or perforation).
 - Ascites.
 - Others—nausea, vomiting, diarrhoea, abdominal pain, mild hepatosplenomegaly.
7. Haematological:
 - Anaemia (normocytic normochromic) and Coombs positive autoimmune haemolytic anaemia.
 - Thrombocytopaenia (often confused with ITP), leucopaenia, neutropaenia and lymphopaenia.
8. Central nervous system (CNS):
 - Fatigue, headache, poor concentration.
 - Visual hallucination.
 - Chorea.
 - Epilepsy.
 - Migraine.
 - Cerebrovascular disease (CVD).
 - Organic psychosis.
 - Paralysis.
 - Depression.
 - Transverse myelitis.
 - Lymphocytic meningitis.
 - Cerebellar ataxia.
 - Cranial nerve palsy.
 - Peripheral neuropathy.
9. Kidneys:
 - Glomerulonephritis (commonly proliferative, may be mesangial, focal or diffuse, and membranous).
 - Nephrotic syndrome.
 - Renal vein thrombosis.
10. Others: Lymphadenopathy, infertility, abortion, menorrhagia.

Q: What are the **types** of SLE?

A: As follows:

1. According to presence of **ARA criteria:**
 - Possible SLE—when 2 criteria are present.
 - Probable SLE—when 3 criteria are present.
 - Definite SLE—when 4 or more criteria are present.
 - Classic SLE—when many criteria are present.
2. According to the **severity:**
 - **Mild:**
 - Fever.
 - Arthralgia, arthritis.
 - Rash, headache.
 - Mild pericarditis or mild pericardial effusion.
 - Mild pleural effusion.

- **Severe:**
 - Massive pleural effusion.
 - Massive pericardial effusion.
 - Renal involvement.
 - CNS involvement.
 - Acute vasculitis.
 - Myocarditis.
 - Lupus pneumonitis.
 - Haemolytic anaemia.
 - Thrombocytopaenic purpura.

Q: What are the **diagnostic criteria** of SLE?

A: As follows:

1. Malar rash.
2. Discoid rash.
3. Photosensitivity.
4. Oral ulcer (oral or nasopharyngeal ulcer, which may be painless).
5. Arthritis (non-erosive arthritis involving two or more peripheral joints with tenderness, swelling or effusion).
6. Serositis:
 - Pleurisy or pleural effusion.
 - Pericarditis or pericardial effusion.
7. Renal involvement:
 - Persistent proteinuria >0.5 g per day (in 24-hour urinary protein) **or**
 - Greater than 3 + proteinuria (if total urinary protein is not performed) **or**
 - Cellular casts (red cell, granular and tubular).
8. Neurological disorder: Seizure or psychosis in the absence of offending drug or metabolic derangement (uraemia, ketoacidosis and electrolyte imbalance).
9. Haematological disorders:
 - Haemolytic anaemia **or**
 - Leucopaenia (<4,000/mm^3 at two or more occasions) **or**
 - Lymphopaenia (<1,000/mm^3 at two or more occasions) **or**
 - Thrombocytopaenia (<100,000/mm^3 in the absence of offending drug).
10. Immunological disorders:
 - Anti-DNA antibody in abnormal titre **or**
 - Anti-Sm antibody (the presence of antibody to Sm nuclear antigen) **or**
 - Positive anti-phospholipid antibody.
 - False-positive serological tests for syphilis (positive for at least 6 months and confirmed by *Treponema pallidum* immobilization or fluorescent treponemal antibody absorption test).
11. **ANA** positive (in the absence of drugs causing lupus syndrome).

N.B. Presence of **four or more** criteria at a time or sequential appearance is diagnostic. Positive anti-double-stranded DNA and anti-Sm (Smith) antibodies are diagnostic of SLE.

Q: What is **'disseminated lupus erythematosus' (DLE)**?

A: It is a variant of SLE in which the disease is mainly limited to skin, characterized by photosensitivity, discoid rash, erythema, scaling, follicular plugging and telangiectasia. M:F = 1:2 (in SLE, the ratio is 1:9). SLE may occur in 5% cases (more in children). ANA is positive (30% cases), anti-double-stranded DNA is negative and complements are normal.

Treatment:

- Hydroxychloroquine 200–400 mg/day.
- In severe cases, prednisolone.
- Use of sunscreen and topical steroid may help.

Q: What is **SCLE (subacute cutaneous lupus erythematosus)**?

A: It consists of scaly red patch or circular, flat, red lesions (confused with psoriasis), highly photosensitive. Most patients have anti-Ro (SSA).

Q: What is the **type of arthritis** in SLE?

A: Usually non-erosive and non-deforming. Rarely, deformity may occur similar to RA called Jaccoud arthritis. Aseptic necrosis of hip and knee may occur.

Q: What are the **atypical features** of SLE?

A: As follows:

- Raynaud phenomenon.
- Chorea.
- Only repeated abortion.
- Epilepsy or cerebrovascular accident (CVA) in young age.
- Psychiatric disorder.

Q: What are the **drugs** causing SLE? What are the **features** of drug-induced SLE? How to **treat** such case?

A: As follows:

- Hydralazine (common [90%] and slow acetylator).
- Procainamide (rapid acetylator).
- Anticonvulsant (carbamazepine and phenytoin).
- Phenothiazine.
- Isoniazid (INH).

- Oral contraceptive pill
- ACE inhibitor.
- Penicillamine.
- Methyldopa.
- Minocycline.

Features of drug-induced SLE:

- Sex ratio: equal.
- Lung involvement is common, but renal and neurological involvements are rare.
- ANA is usually positive.
- Anti-double-stranded DNA is negative.
- Complements are normal.
- Anti-histone antibody is positive in 95% of the cases (characteristic, but not specific).
- Drugs causing SLE-like syndrome usually do not aggravate primary SLE.
- Clinical features and laboratory abnormalities revert to normal when the offending drugs are withdrawn.

Treatment: Withdrawal of drugs. Short course of steroid is necessary.

Q: What is the relation of **pregnancy with SLE**?

A: Pregnancy is not contraindicated. Fertility is usually normal except in severe disease. Repeated abortion (due to the presence of anti-phospholipid antibody), still birth and intrauterine growth retardation may occur.

The disease should be in remission and pregnancy should be avoided if there is neurological, renal and cardiac abnormality. Relapse may occur in the first trimester and in puerperium.

If the mother has **'anti-Ro antibody'** (SSA), there may be congenital complete heart block of the baby due to transplacental transfer of antibody. With anti-Ro or anti-La antibodies in mother, there is 2% risk of giving birth to a baby with neonatal lupus syndrome. This is characterized by skin rash, hepatitis and fetal heart block.

Treatment of SLE during pregnancy: Prednisolone should be continued (avoid dexamethasone and betamethasone, which are broken by placental enzymes).

Q: What is the cause of **abdominal pain in SLE**?

A: As follows:

- Mesenteric vasculitis or perforation of gut.
- Peptic ulcer as a complication of steroid.
- Perisplenitis or splenic infarction.
- Pancreatitis.

Q: What is the **type of arthritis** in SLE?

A: Usually non-erosive and non-deforming. Rarely, deformity may occur similar to RA called Jaccoud arthritis. Aseptic necrosis of head of femur may occur.

Q: What is the cause of **avascular necrosis** of head of femur in SLE?

A: It is due to:

- Vasculitis in SLE.
- Prolonged use of steroid therapy (actual cause of necrosis due to steroid is unknown. Probably steroid causes hypertrophy of lipocytes, which compresses blood vessels, leading to ischaemic necrosis of bone).

Q: What is the cause of **backache** in SLE?

A: Avascular necrosis, which is due to vasculitis and steroid therapy. Avascular necrosis is the ischaemic necrosis of bone. It commonly involves head of femur, also knee, shoulder and so on.

Q: What **investigations** should be done in SLE?

A: As follows:

1. CBC (anaemia, leucopaenia, thrombocytopaenia, lymphopaenia and high ESR).
2. Urine (proteinuria, haematuria, and RBC or granular cast). If proteinuria is present, 24 hour urinary protein should be done.
3. CRP (It is normal. If CRP is increased, it indicates infection).
4. ANA (positive in 95% cases. It is the most sensitive screening test).
5. Anti-double-stranded DNA (positive in 30–50% of the cases. It is highly specific for SLE).
6. Anti-Sm (Smith) antibody (positive in 10–25% cases).
7. Complements (C3 and C4 are low in active disease).
8. Immunoglobulin (high titre of IgM and IgG).
9. Serum anti-phospholipid antibody (detected by enzyme-linked immunosorbent assay, ELISA).
10. Others (these indicate presence of antiphospholipid antibody):
 - VDRL (false positive).
 - Platelet (low).
 - Prothrombin time (prolonged).
 - APTT (prolonged, not corrected by addition of normal plasma).
11. Skin biopsy (from normal skin and skin lesion for histopathology and DIF):
 - Normal skin biopsy—immunofluorescence test shows deposition of immune complex at dermoepidermal junction (lupus band).

Biopsy specimen of normal skin for DIF should be sent in normal saline soaked gauge (not in formalin, as the protein is denatured by formalin). For histopathology, biopsy specimen is taken in formalin.

12. If renal involvement : 24 hours urinary protein, serum urea and creatinine, creatinine clearance rate (CCR), renal biopsy.
13. If CNS involvement: EEG, CT or MRI.

Q: What are the features of **renal involvement** in SLE?

A: Renal involvement occurs in 1/3rd of SLE; of these, 25% develop end-stage renal failure within 10 years. Lupus nephritis is classified histologically by WHO criteria.

Type	Histology	Clinical features
Type I	**Minimal** mesangial lupus nephritis (LN), normal on light microscopy	Asymptomatic
Type II	**Mesangial** proliferative LN with mesangial hypercellularity and matrix expansion.	Mild renal disease
Type III	**Focal** LN (involving <50% glomeruli). Subepithelial deposits seen.	Haematuria and proteinuria
Type IV	**Diffuse** LN (involving ≥50% glomeruli). There are segmental and global lesions as well as active and chronic lesions. Subendothelial deposits are present.	Progression to nephrotic syndrome, hypertension and renal insufficiency. It is the most common and most severe form of LN.
Type V	**Membranous** LN, occurs in 10–20% patients. Can occur in combination with type III and IV.	Heavy proteinuria (NS), haematuria, hypertension. Good prognosis.
Type VI	Advanced **sclerosing** LN. It causes sclerosis of >90% glomeruli.	Progressive renal failure. Severe form.

Treatment of LN:

- Type I: No treatment.
- Type II: Benign. But sometimes, steroid may be needed.
- Type III, IV and V: Immunosuppressive therapy with steroid and cyclophosphamide or mycophenolate mofetil is used for induction. Then azathioprine and mycophenolate mofetil are used for maintenance.
- Rituximab (anti-CD-20) may be used in some patients.
- Symptomatic treatment for hypertension and oedema.

N.B. Remember the following:

- Focal glomerulonephritis respond well to treatment with prednisolone 40–60 mg/day.
- Diffuse and membranous lesions do not respond well to steroid only. Pulse therapy with methylprednisolone for 3 days followed by maintenance with prednisolone is necessary. Sometimes azathioprine 2–3 mg/kg bodyweight or cyclophosphamide 100–150 mg daily with prednisolone may be given.
- Pulse therapy: IV cyclophosphamide is more effective than pulse methylprednisolone alone. Also, combination therapy is sometimes more effective. Continuing IV treatment, quarterly for 1 year, after renal remission decreases the risk of renal flare.
- Prognosis is better in type I, II and V.

Q: How to **diagnose renal involvement** in SLE?

A: The patient may present with nephrotic syndrome or acute nephritic illness or renal failure. Renal involvement is diagnosed by:

1. Urine:
 - Proteinuria (+++), haematuria, and granular or RBC cast.
 - UTP (24 hours urinary total protein) >0.5g.
2. Blood:
 - Urea and creatinine (high) and creatinine clearance rate (CCR): low.
3. Renal biopsy.

Q: How to **treat** SLE?

A: As follows:

1. **General measures:**
 - Explanation and education regarding the nature of the disease.
 - Reassurance.
 - Psychological support.
 - Avoidance of UV light exposure, use of sun blocks.
 - Cardiovascular risk factors like hypertension and hyperlipidaemia should be controlled. Smoking should be stopped.
2. **Drug therapy:**
 - Mild cases—NSAID (if fever, arthralgia and headache).
 - Chloroquine or hydroxychloroquine—effective in cutaneous lesion, arthritis, arthralgia and serositis without organ involvement.

- Rash, synovitis or pleuropericarditis—short course steroid.
- Severe and active disease—steroid should be given.
- Acute life-threatening SLE affecting kidney, CNS or CVS, haemolytic anaemia, thrombotic thrombocytopaenia—high-dose steroid and immunosuppressive drug. Pulse methylprednisolone (500 mg to 1 g IV) daily for 3–5 days. Cyclophosphamide (2 mg/kg IV) may be given 2–3 weekly on 6–8 occasions.
- In renal involvement—mycophenolate mofetil may be used instead of cyclophosphamide.
- In thrombocytopaenia not responding to immunosuppressive therapy, danazol may be used.

Steroid (prednisolone):

Indications:

- In mild disease, not responding to chloroquine and NSAID.
- Severe and active disease with involvement of organ (heart, kidney, CNS and haematological abnormality).

Dose:

- Without major organ involvement—0.25–0.5 mg/kg/day.
- Major organ involvement—1–1.5 mg/kg/day.

Dose schedule of steroid (one suggested regimen):

- Initially, full dose (45.0–60.0 mg daily) for 4–8 weeks, then
- Reduce 10.0 mg weekly till 30.0 mg, then,
- 25.0 mg/day for 1 week, then,
- 20.0 mg/day for 1 week, then,
- 15.0 mg for 1 month, then,
- Reduce 2.5 mg every 2 weekly as follows—
 - First day 15.0 mg, second day 12.5 mg – 2 weeks, then
 - First day 15.0 mg, second day 10.0 mg – 2 weeks, and so on.
 - This is continued until 2nd day regimen is completed, then
- 15.0 mg on alternate day (continue and follow up).

When the disease activity (both clinically and biochemically) disappears, steroid should be reduced slowly over months and can be withdrawn (may be needed to continue for 2–3 years. For lupus nephritis, treatment is usually given for 5 years).

Methylprednisolone:

Indication: Severe SLE, when there is carditis, renal and cerebral involvement, poor general condition.
Dose: 500 mg to 1 g mixed with 200 mL 5% DA IV daily for 3–5 days, followed by prednisolone 1 mg/kg for 6–10 weeks, then gradual tapering.

Cyclophosphamide:

Indications:

- Renal lupus (classes III, IV and V).
- Severe renal disease as evidenced by (UTP > 1 g, raised serum creatinine and decreased creatinine clearance).
- CNS involvement.

Dose:

- 0.5–1 g/m^2 of body surface area. It is given monthly as a pulse therapy IV with 500 mL fluid (every month for six cycles, then every 3 months for another six cycles or till the disease is inactive for 1–2 years). Then hydroxychloroquine or azathioprine can be started.
- Alternately, cyclophosphamide 250 mg/m^2 of body surface may be given every 15 days for 12 doses, followed by prednisolone as maintenance therapy.
- Oral cyclophosphamide can be given.
- After 12 weeks of cyclophosphamide, oral azathioprine (2–2.5 mg/kg daily) may be given.
- Advantages of azathioprine—no gonadal toxicity and no adverse effect on pregnancy.
- Cyclophosphamide can cause gonadal toxicity, amenorrhoea, sterility, premature menopause and sometimes, leukaemia may occur. Moreover, it cannot be continued in pregnancy.
- Cyclophosphamide is usually given with high-dose prednisolone.

(Periodic blood count should be done initially 2 weekly, then monthly.)

Q: What is the **mechanism of haemorrhagic cystitis**? How to **prevent** this?

A: Cyclophosphamide can cause haemorrhagic cystitis (more by oral route). It is due to production of **acrolein**, a metabolite from cyclophosphamide that is highly toxic to the mucosa of the urinary bladder.

This can be prevented by:

- Plenty of fluid (3–4 L).
- Using mesna (0, 4 and 8 hours of therapy).
- Advise the patient to micturate frequently.

Prognosis in SLE:

- 10-year survival rate is 90%, but this is lower if vital organs are involved (heart, kidney, lung, CNS).
- Mortality shows bimodal pattern. In early age, death is usually due to infection (mostly opportunistic), renal or cerebral disease. In later age, accelerated atherosclerosis is common, incidence of myocardial infarction is 5 times more than in general population (so, risk factor for atherosclerosis should be avoided, such as avoid smoking, control hypertension, obesity, hyperlipidaemia etc.).
- In the long term, some patients may develop cancers, especially lymphoma.
- Rarely, there may be deforming arthritis, chronic progressive destruction of joints and osteoarthrosis.

Q: What is **anti-phospholipid syndrome?**

A: Anti-phospholipid syndrome is characterized by the presence of anti-phospholipid antibody, associated with recurrent arterial or venous thrombosis, recurrent fetal loss or thrombocytopaenia. Some patients with anti-phospholipid antibody may not get anti-phospholipid syndrome. It is positive in SLE and may be found in many other cases, but may be positive without any cause, called primary anti-phospholipid syndrome.

Two types of anti-phospholipid antibody:

- Anticardiolipin antibody—may be IgG or IgM. IgG is more pathogenic.
- Lupus anticoagulant—it interferes with phospholipid-dependent coagulation tests.

In some patients, only one of these is positive and in others, both are positive.

Presence of anti-phospholipid antibody is associated with:

- Thrombosis, venous or arterial; 17% of stroke <45 years of age is thought to be due to anti-phospholipid antibody.
- Recurrent abortion or intrauterine growth retardation.
- Haematological—thrombocytopaenia and autoimmune haemolytic anaemia.
- Neurological—epilepsy, TIA, stroke, migraine and chorea.
- Heart—sterile endocarditis (Libman–Sacks).
- Renal involvement with proteinuria and lupus nephritis (membranous).
- Skin-ulceration, livedo reticularis, gangrene and necrosis of digit.

It is of two types:

1. Primary: Thromboembolism without features of SLE.
2. Secondary: Causes are—
 - Rheumatological—SLE, DLE, RA, systemic sclerosis, Sjögren syndrome, psoriatic arthropathy, dermatomyositis.
 - Vasculitis—Behcet syndrome, temporal arteritis, Takayasu arteritis.
 - Malignancy—solid tumours like bronchial carcinoma, hypernephroma, prostatic carcinoma, thymoma, oesophageal carcinoma.
 - Haematological disease—leukaemia, lymphoma, myelofibrosis, polycythaemia, myeloma, monoclonal gammopathy.
 - Infections—HIV, infectious mononucleosis, rubella, parvovirus, hepatitis, TB, leprosy, infective endocarditis, Klebsiella, syphilis.
 - Drug induced—procainamide, phenothiazine.
 - Miscellaneous—diabetes mellitus, dialysis patient.

In <1% cases of anti-phospholipid syndrome, a severe type called catastrophic anti-phospholipid syndrome may occur. In such case, there may be diffuse thrombosis, thrombotic microangiopathy and multiorgan failure. It is treated with intravenous heparin, high-dose steroid and intravenous immune globulin and plasmapheresis.

Investigations:

1. Serum anti-phospholipid antibody (anti-cardiolipin and lupus anticoagulant).
2. Indirect tests for anti-phospholipid antibody (anticoagulant):
 - Thrombocytopaenia.
 - False positive VDRL.
 - Prolonged prothrombin time.
 - Prolonged APTT, which is not corrected by addition of normal plasma.

Treatment anti-phospholipid syndrome:

- With thrombosis: Warfarin should be continued for life long.
- Without history of thrombosis, but with anti-phospholipid antibody only: Aspirin or clopidogrel may be given. Rarely warfarin may be needed.
- In pregnancy: Low-dose aspirin and subcutaneous heparin should be started early in gestation. This reduces the chance of miscarriage, but pre-eclampsia and poor fetal growth remain common.

Vasculitis

Usual instructions are:

- Perform the general examination.
- Look at the foot or hand.

Presentation of a Case

- There are few infarctions at the tip of the great and second toe of right foot, also one small infarction at the tip of small toe of left foot.
- Multiple purpuric spots and few papular lesions are present on the front of both legs.
- There is one small ulcer above the medial malleolus.

My diagnosis is **vasculitis**.



Vasculitis (toes)



Vasculitis (fingers)

Q: What **else** do you like to see?

A: I want to see any evidence of collagen disease like rheumatoid arthritis, SLE (butterfly rash, alopecia), history of fever, hypertension, heart (infective endocarditis), history of drug therapy.

N.B. If vasculitis is associated with deformity of hand or foot joint, likely diagnosis is rheumatoid arthritis with vasculitis.

Q: What are the **differential** diagnoses?

A: As follows:

- Drug reaction.
- Collagen disease (SLE, rheumatoid arthritis, Wegener granulomatosis, polyarteritis nodosa).
- Microscopic polyarteritis.
- Cryoglobulinaemia.
- Buerger disease.
- Henoch–Schönlein purpura.
- Sarcoidosis.
- Cutaneous amyloidosis.

Q: What are the **diseases** that mimic vasculitis?

A: As follows:

- Infective endocarditis.
- Meningococcaemia.
- Atrial myxoma.
- Anti-phospholipid syndrome.
- Malignancy.
- Cholesterol emboli.

Q: What is **vasculitis**?

A: Vasculitis syndrome is a heterogeneous group of disorders characterized by inflammation and necrosis of the walls of affected blood vessels, with associated damage to the skin, kidney, lung, heart, brain and gastrointestinal tract. Vasculitis may be primary in the absence of any cause or secondary to many inflammatory or infective diseases.

Q: What are the common **causes** of vasculitis?

A: Causes of vasculitis depend on the type of artery affected.

1. Involvement of large artery:
 - Giant cell arteritis, polymyalgia rheumatic.
 - Takayasu arteritis.
 - Behcet disease.
2. Involvement of medium-sized artery:
 - Classical polyarteritis nodosa.
 - Buerger disease.
 - Kawasaki disease.
3. Involvement of small artery:
 - Immune complex mediated—Henoch–Schönlein purpura, essential cryoglobulinaemia, cutaneous leucocytoclastic vasculitis.
 - ANCA associated—Wegener granulomatosis, Chug–Strauss syndrome, microscopic polyangiitis.

4. Other conditions associated with vasculitis:
 - Drug-induced vasculitis.
 - Infective, e.g. subacute bacterial endocarditis, chronic hepatitis B and C.
 - Collagen disease—rheumatoid arthritis, SLE, systemic sclerosis, polymyositis or dermatomyositis.
 - Goodpasture syndrome.
 - Hypocomplementaemia.
 - Serum sickness.
 - Vasculitis with malignancy (paraneoplastic syndrome)—lymphoma, hairy cell leukaemia.
 - Inflammatory bowel disease.

Q: What are the common **clinical features** of vasculitis?

A: As follows:

1. Constitutional symptoms: Fever, weight loss, malaise, arthralgia, arthritis, myalgia.
2. Features due multiple systems of the body:
 - Skin—painful palpable purpura, vesiculobullous lesions, urticaria, cutaneous nodules, ulcers, livedo reticularis, digital gangrene.
 - Eye—episcleritis, ulcer, visual loss.
 - Ear, nose, throat—epistaxis, nasal crust, recurrent sinusitis, deafness.
 - Respiratory—haemoptysis, cough, dyspnoea.
 - Cardiac—heart failure, angina or myocardial infarction.
 - Gastrointestinal—abdominal pain (due to chronic ischaemia or mucosal inflammation), mouth ulcer, diarrhoea.
 - Renal—proteinuria, haematuria, cast, acute or chronic renal failure.
 - Neurological—mononeuritis multiplex, sensory or motor neuropathy, fit, psychoses, confusion, stroke.
3. Secondary vasculitis: Features of the primary disease.

Q: What **investigations** should be done?

A: As follows:

- CBC, ESR.
- CRP.
- Urine for routine examination.
- ANA, anti-ds-DNA, pANCA, cANCA.
- Biopsy of involved organ for histology and immunofluorescence.
- Angiography in some cases.

Q: How to **treat** vasculitis?

A: As follows:

- According to the cause.
- High-dose steroid and immunosuppressive drugs are given in many cases.

Osteoarthrosis

Usual instruction:

- Look at the patient's hands; Or, examine the hands of this patient.

Presentation of a Case

- There are bony swellings at the proximal (Bouchard nodes) and distal (Heberden nodes) interphalangeal joints of both hands.
- DIP joints of both hands are swollen.

My diagnosis is **osteoarthrosis**.



Osteoarthrosis of hands



Osteoarthrosis of knees

Q: Why osteoarthrosis?

A: Because Bouchard and Heberden nodes are hallmarks of osteoarthrosis.

Q: What are Bouchard and Heberden nodes?

A: As follows:

- Bouchard node is the new bone formation at the proximal interphalangeal joint.

- Heberden node is the new bone formation at the distal interphalangeal joint.

Q: **What else** do you want to see?
A: I want to examine other joints, especially the knee joints, ankles, cervical and lumbar spine.

Q: What are the x-ray **findings**?
A: Osteophyte, also marginal sclerosis may be seen.

Q: What is **osteoarthrosis**?
A: It is a degenerative disease of the synovial joint characterized by focal loss of articular hyaline cartilage with proliferation of new bone and remodelling of joint contour. It is not inflammatory.

Q: What are the **types** of osteoarthrosis?
A: Two types:
- Primary.
- Secondary—usually asymmetrical, commonly involve the weight-bearing joints. Causes are trauma, rheumatoid arthritis, septic arthritis, gout, neuropathic joints, acromegaly, hyperparathyroidism, chondrocalcinosis, haemochromatosis.

Q: What is **nodal** osteoarthrosis?
A: It is a primary generalized osteoarthrosis, which is autosomal dominant and occurs mainly in middle-aged women. There may be bilateral symmetrical involvement of many joints. Bouchard and Heberden nodes are typically found in nodal osteoarthrosis. There is good functional outcome of the hands despite marked deformity.

Q: What are the **complications** of osteoarthrosis?
A: As follows:
- Entrapment of nerves (like ulnar nerve), carpal tunnel syndrome.
- Cervical spondylosis.
- Deformity.

Q: What typical **deformity** may occur in the hand?
A: Square hand due to subluxation of the first metacarpophalangeal joint.

Q: In the hand, which **joint** is typically involved in osteoarthrosis?
A: Distal interphalangeal joints (DIP).

Q: What are the diseases that involve **DIP**?
A: As follows:
- Osteoarthrosis.
- Psoriatic arthritis.
- Gout.

Q: How to **treat** osteoarthrosis?
A: As follows:
- Explanation and reassurance.
- Patient education.
- Regular exercise.
- Reduction of adverse mechanical factors, e.g. weight reduction if obese, use of appropriate footwear, walking stick etc.
- Pain relief—paracetamol, topical or oral NSAID and capsaicin are used. Intra-articular corticosteroid may be needed.
- Physiotherapy may be helpful.
- Surgery includes osteotomy and joint replacement.

Charcot Joint

Usual instruction:

- Look at the patient's knee or ankle joint or examine the lower limb.

Presentation of a Case

- The right ankle joint is swollen and deformed.
- Movement of the right ankle produces crepitus sounds.

My diagnosis is **Charcot joint**.



Charcot joint of both knee

Q: What **else** do you like to see or what history do you like to take?

A: As follows:

- Sensory examination.
- In the upper limb, dissociated sensory loss (to exclude syringomyelia).
- History of lancinating pain, signs of posterior column lesion and Argyll Robertson pupil (to exclude tabes dorsalis).
- History of diabetes mellitus.

Q: What is **Charcot joint**? What are the **causes**?

A: It is the complete destruction and disorganization of the joint, usually secondary to loss of proprioception of the joint sense.

Causes are:

- Syringomyelia (usually involves joint of upper limb—elbow, shoulder joint).
- Tabes dorsalis (usually involves joint of lower limb—knee, ankle).
- Diabetes mellitus (usually involves the joint of foot).
- Leprosy.
- Repeated intra-articular injection of steroid.
- Others—meningomyelocele, hereditary sensory neuropathy, peripheral nerve injury etc.

Q: What are the **x-ray** findings?

A: As follows:

- Reduction, destruction and disorganization of the joint.
- Loose bodies.
- Marginal sclerosis.



X-ray of Charcot joint of knee

CHAPTER 10

EXAMINATION OF THE EYE

"To all students of medicine – who listen, look, touch and reflect: may they hear, see, feel and comprehend"

– Barlow

Introduction

Usual instructions are:

- Examine the fundus. What are your findings?
- Examine the eye of this patient.
- Look at the eyes. What are your findings? (May be ptosis, exophthalmos, squint, xanthelasma and heliotrope rash.)

Proceed as follows:

Before examining the eyes, patient should sit at the edge of the bed facing the examiner.

Inspection:

1. Look at the face to see any facial asymmetry (in hemiplegia and Bell palsy), myasthenic, myotonic, tabetic face, and thyrotoxic or hypothyroid face.
2. Ptosis (complete or partial), squint, exophthalmos, eyebrows (fall of lateral one-third), xanthelasma, lid retraction, puffy face with baggy eyelids and heliotrope rash.
3. Cornea (arcus, Kayser–Fleischer [KF] ring, band keratopathy, ulceration and Bitot spot).
4. Sclera (blue sclera, pigmentation, redness and chemosis).
5. Pupil:
 - Size (dilatation or constriction).
 - Shape (irregular or unequal).
 - Light reflex (direct and consensual).
 - Accommodation reflex.
6. Movement of the eyeball:
 - Keep the head of the patient fixed. Tell the patient: "Follow my finger".
 - See both horizontally and vertically like "**H**".
 - During the movement of eyes: Look for nystagmus, diplopia (by asking the patient at the extreme gaze), lid lag and lid retraction.
7. Look for:
 - Acuity of vision (for distant and near vision).
 - Colour vision.
 - Field of vision.
 - Corneal reflex.
8. Finally, **perform** fundoscopy.
 For **fundoscopy**, proceed as follows:
 - The patient should be examined either in sitting or lying down in a dark room.
 - Ask the patient to look straight and keep his or her eyes open.
 - Candidates should use his or her right or left eye to examine the patient's corresponding eye.
 - Look at the eye from at least 50 cm and check for red reflex (start with 201 red numbers). Opacity in media of the eye (cornea, anterior chamber, lens and vitreous) will appear as black specks or lines against red reflex.
 - Look at the following points by gradually coming from red numbers to black (negative) and ophthalmoscope brought close to the patient's eye:
 - Optic disc (comment on colour, margin and cup).
 - Macula (one or two discs away from and a little below the temporal margin of the disc). It appears darker than the surrounding retina and in young individuals has a central yellow point called "fovea centralis".
 - See the nasal and temporal halves of fundus and then the whole fundus.
 - Look for retinal vessels (remember, retinal artery has four main branches and normal ratio of artery to vein is 2:3).
 - Look for transparency of vessels (arteries usually have a shiny central reflex stripe),

presence of arteriovenous (AV) nipping and tortuosity of veins.
- Look for exudate and haemorrhage.

Present your findings systematically.

Normal optic disc: Rich in yellow colour, rest of fundus is rich in red colour.



Normal fundus



Bilateral ptosis

Optic Atrophy

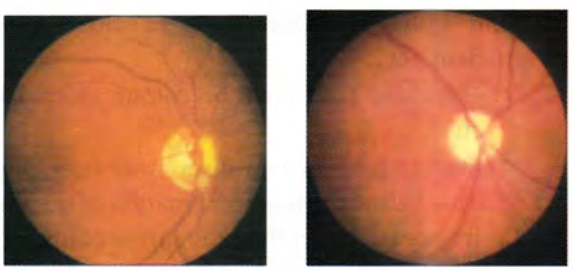
Usual instructions are:

- Examine the fundus. What are your findings?

Presentation of Case No. 1

(Mention in which eye—right or left or both)
- The disc is pale with clear margin.
- There is reduction of number of capillaries in the disc (normally 7–10 capillaries cross the disc margin).
- No other changes in retina.

My diagnosis is **primary optic atrophy (OA)**.



Primary optic atrophy

Q: Why primary OA?
A: Because, the disc is pale with clear margin and no change in retina.

Q: Why not secondary OA?
A: In secondary OA:
- Disc: greyish white.
- Margin: indistinct.
- Some changes in retina may be present (e.g., exudate and haemorrhage).

Q: What is the mechanism of OA?
A: Degeneration of optic nerve fibres.

Q: What do you think are the causes in this patient?
A: As follows:
- Intracranial space-occupying lesion (SOL).
- Secondary to optic neuritis (multiple sclerosis).
- Glaucoma.
- Optic nerve compression (by tumour and aneurysm).

Presentation of Case No. 2

- The disc is greyish-white with indistinct margin.
- There are few exudates and haemorrhage in the retina (mention the location).

My diagnosis is **secondary** OA.



Secondary optic atrophy



Secondary optic atrophy

Q: Why **secondary** OA?

A: Because:

- Disc is greyish-white with indistinct margin.
- There is exudate and haemorrhage in the retina.

Q: What do you think is the **cause** of secondary OA?

A: Secondary to papilloedema.

Q: How do you **investigate** in a case of OA?

A: As follows:

- Full blood count (FBC) and peripheral blood film (macrocytic anaemia in vitamin B_{12} deficiency).
- Serological test for syphilis (venereal disease research laboratory [VDRL] and *Treponema pallidum* haemagglutination TPHA).
- X-ray of the skull.
- Computed tomography (CT) or magnetic resonance imaging (MRI) of brain.
- Other investigations according to suspicion of causes.

Q: What are the types of OA?

A: There are three types:

- Primary (due to optic neuritis, compression in the optic nerve and glaucoma).
- Secondary (to papilloedema, as in intracranial SOL).
- Consecutive (secondary to the disease of retina: retinitis pigmentosa, choroidoretinitis and Tay–Sach disease).
 (The term consecutive is controversial; it is **actually** a secondary OA.)

Q: What are the **causes** of OA?

A: As follows:

1. Raised intracranial pressure due to intracranial SOL (neoplasm, abscess and cyst).
2. Long-standing papilloedema.
3. Secondary to optic neuritis, which may be due to:
 - Demyelinating disease.
 - Drugs (ethambutol, quinine and chloroquine) and toxins (methyl alcohol poisoning, lead, arsenic and cyanide poisoning).
 - Neurosyphilis.
 - Nutritional amblyopia (vitamin B_{12} deficiency, tobacco and alcohol).
4. Hereditary (Friedreich ataxia, Leber OA and DIDMOAD syndrome).
5. Ischaemic optic neuropathy (in giant cell arteritis).
6. Others: Trauma in optic nerve, Paget disease and retinal artery occlusion.

Q: What is DIDMOAD syndrome?

A: It is the combination of:

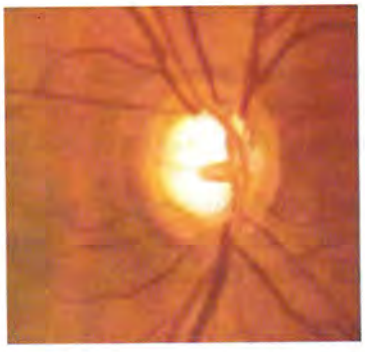
- **DI:** Diabetes insipidus.
- **DM:** Diabetes mellitus.
- **OA:** Optic atrophy.
- **D:** Deafness.

Q: What is **glaucomatous** OA?

A: Glaucomatous OA denotes loss of disc substance; hence, cup is enlarged and emerging vessels appear to bend sharply outwards.



Glaucomatous optic atrophy (advanced, severe)



Glaucomatous optic atrophy (early)

Q: What is the **difference** between optic neuritis and optic atrophy?

A: Optic neuritis is an acute inflammatory process affecting the optic nerve. Optic atrophy is the degeneration of the optic nerve head, sometimes a sequel to optic neuritis.

Papilloedema (Pure)

Usual instructions are:

- Examine the fundus. What are your findings?

Presentation of a Case

(Mention in which eye, right or left or both)

- There is bilateral papilloedema, more marked in right or left eye.

Q: What do you think is the **cause** in this case?

A: Possible causes are (in the absence of exudate or haemorrhage or other changes in retina):

- Raised intracranial pressure due to SOL (neoplasm, abscess and haematoma).
- Benign intracranial hypertension.

Q: Could it be **malignant hypertension**?

A: Unlikely, because in malignant hypertension there will be other changes of hypertensive retinopathy, such as, AV nipping, exudate and flame-shaped haemorrhage.

Q: Which disease is **confused** with papilloedema?

A: It is confused with:

- Papillitis (optic neuritis).
- Pseudopapilloedema (developmental anomaly of the optic nerve and there is no oedema. It has no clinical significance).
- Drusen (hyaline bodies): Pale yellow spots, mostly in macula.
- Myelinated nerve fibres.

N.B. If confusion arises, it may be confirmed by fluorescence angiography. In papilloedema, leaking of the dye in capillaries occur.

Q: What is the **visual abnormality** in papilloedema?

A: Transient obscurations of vision due to temporary impairment of retinal blood flow.

Q: What is the **field defect** in papilloedema?

A: Peripheral constriction of visual field and blind spot is enlarged.

Q: What is the important **sign** in papilloedema due to raised intracranial tension?

A: Absence of venous pulsation.

Q: What is **papilloedema**? What are the **stages** of papilloedema?

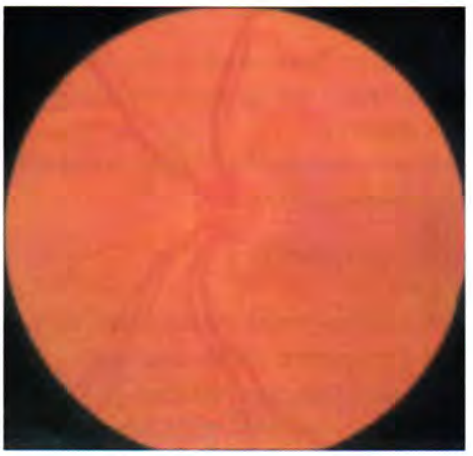
A: It is the swelling of the optic nerve head. Stages are:

- Early sign: Absence of spontaneous pulsation of retinal veins and increased pink or red colouration of the disc.
- Blurring of disc margin, first starting in nasal side.
- Filling of physiological cup.
- Fullness of optic disc, then elevation.
- Vessels on the disc become curved over its edge.
- May be haemorrhage surrounding the disc.

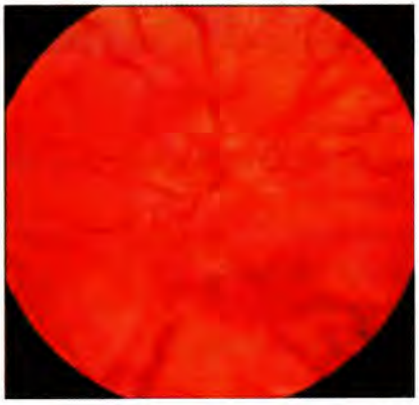
Q: What are the **differences** between papillitis (optic neuritis) and papilloedema?

A: As follows:

Features	Papillitis (optic neuritis)	Papilloedema
Eye	Painful, specially on movement	No pain
Visual acuity	Markedly reduced	Slightly reduced in advanced cases
Colour vision	Affected (red)	Normal
Central scotoma	Present	Absent, and there is peripheral constriction of visual field
Blind spot	Normal	Increased
Pupil	Dilated, less reaction to bright light	Normal



Papilloedema (early)



Papilloedema (advanced case showing blurring of margin and bleeding)

Q: What are the causes of **papilloedema**?

A: As follows:

1. Raised intracranial pressure due to any cause (such as intracranial space occupying lesion, intracranial haemorrhage, venous sinus thrombosis, cerebral oedema, hydrocephalus, meningitis, encephalitis).
2. Hypertensive retinopathy (malignant hypertension).
3. Benign (idiopathic) intracranial hypertension.
4. Central retinal vein occlusion.
5. Others:
 - CO_2 retention (hypercapnia).
 - Subarachnoid haemorrhage or cerebrovascular accident (CVA).
 - Secondaries in brain.
 - Guillain–Barré syndrome.
 - Graves disease.
 - Cavernous sinus thrombosis.
 - Severe anaemia.
 - Hypoparathyroidism or hypocalcaemia.
 - Hypervitaminosis A.

Q: What are the causes of **unilateral papilloedema**?

A: As follows:

- Central retinal vein occlusion.
- Foster–Kennedy syndrome. Infiltration in one eye (lymphoma, leukaemia and sarcoidosis).
- Early stage of bilateral papilloedema.

Q: What is **Foster–Kennedy** syndrome?

A: It is characterized by a frontal lobe tumour compressing optic nerve causing ipsilateral optic atrophy but contralateral papilloedema due to raised intracranial pressure.

Q: What is **benign (idiopathic) intracranial hypertension (BIH)**? What are the **causes**?

A: It is a syndrome of raised intracranial tension in the absence of intracranial SOL, localizing neurological sign or cerebrospinal fluid (CSF) out-flow obstruction. Common in females of 18–40 years of age, obese and rarely familial. Its causes are:

- Drugs: Tetracycline, nalidixic acid, oral contraceptive pill, nitrofurantoin, sulphur drugs, phenytoin and steroid (both therapy and withdrawal).
- Endocrine disorders: Hyperthyroidism, hypothyroidism, hypoparathyroidism, Addison disease and Cushing syndrome.
- Others: Hypervitaminosis A, pregnancy, menarche, puerperium, middle ear disease, dural sinus thrombosis or obstruction, head injury, systemic lupus erythematosus (SLE), and cryoglobulinaemia.

Q: What is the commonest **presentation** of BIH?

A: Frequent headache.

Q: What is the **complication** of BIH?

A: Visual loss.

Q: How to **diagnose** BIH? What **investigations** do you suggest?

A: Diagnosis is done by exclusion of other diseases. Investigations are:

- X-ray of the skull (increased size of sella turcica).
- Lumbar puncture shows increased CSF pressure and no other changes in CSF.
- CT or MRI of brain (to exclude other pathology).
- Sometimes, MR angiography or cerebral venography may be done to exclude cerebral venous sinus thrombosis.

Q: How to **treat** BIH?

A: As follows:

1. Treatment of predisposing factors (reduce obesity and avoid precipitating drug).
2. Frusemide or acetazolamide, steroid may be given.
3. Frequent lumbar puncture (may be done on alternate days).
4. If no response:
 - Lumboperitoneal shunt, especially, if progressive visual loss.
 - Optic nerve sheath fenestration may be done.

Central Retinal Vein Occlusion (CRVO)

Usual instructions are:

- Examine the fundus. What are your findings?

Presentation of Case No. 1

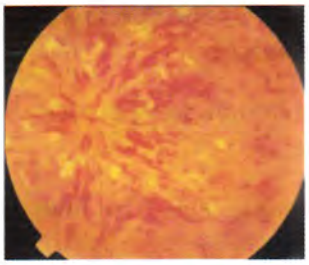
(Mention in which eye, right or left)

- There are multiple scattered haemorrhages over the whole retina.
- The veins are dilated and tortuous.
- Few soft exudates and papilloedema are present.

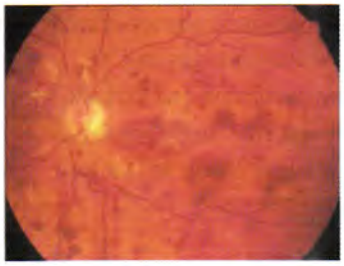
My diagnosis is **central retinal vein occlusion (CRVO)**.

Q: What is the **appearance** of haemorrhage in CRVO?

A: Stormy sunset appearance.



Central retinal vein occlusion (bleeding with multiple exudate)



Central retinal vein occlusion (more severe—with multiple bleeding)

Q: What are the **causes** of CRVO?

A: As follows:

- Hypertension (the commonest cause, 70% cases).
- Atherosclerosis.
- Diabetes mellitus (DM).
- Hyperviscosity syndrome (causes are multiple myeloma, Waldenstrom macroglobulinaemia and polycythaemia rubra vera).
- Others: Leukaemia, hyperlipidaemia, nephrotic syndrome, SLE, antiphospholipid syndrome, hypercoagulable state (antithrombin III deficiency, protein S or C deficiency, factor V Leiden mutation) etc.

Q: What are the **complications** of CRVO?

A: As follows:

- Neovascularization of retina (may require laser therapy).
- Rubeosis iridis.
- Glaucoma (rubeotic).
- Optic atrophy.
- Permanent loss of vision.

Q: What is the **prognosis** of CRVO?

A: As follows:

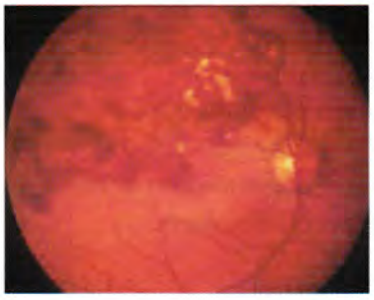
- In mild case without macular involvement, there is no visual disturbance.
- In severe case, there is marked visual deterioration. Secondary glaucoma may occur due to new vessels formation.

Presentation of Case No. 2

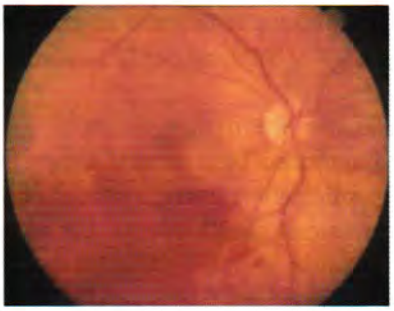
(Mention in which eye, right or left)

- There are multiple scattered haemorrhages over the right lower part of the retina.
- The veins are dilated and tortuous.
- Few soft exudates and papilloedema are present.

My diagnosis is **branch retinal vein occlusion**.



Branch retinal vein occlusion (involving the upper part; bleeding with some exudate)



Branch retinal vein occlusion (involving the lower part; only bleeding, no exudate)

Q: What is the prognosis in **branch retinal vein occlusion?**

A: Prognosis is good, if haemorrhage does not involve macula.

N.B. Superior temporal vein is commonly involved. There may be quadrantic field defect.

Q: What **investigations** do you suggest in central retinal vein occlusion?

A: As follows:

- Full blood count.
- Blood sugar.
- Bone marrow (to exclude multiple myeloma).
- Plasma viscosity.
- Plasma protein electrophoresis.
- Lipid profile.

Q: How to treat?

A: Treatment of primary cause.

Hypertensive Retinopathy

Usual instructions are:

- Examine the fundus. What are your findings?

Presentation of Case No. 1

(Mention in which eye, right or left)

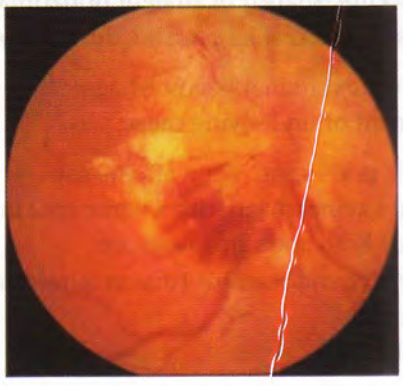
- Retinal arterioles are irregular, tortuous and narrow.
- There is silver wiring with increased light reflex.
- Veins are engorged, and AV nipping is present.
- There are flame-shaped haemorrhages and cotton-wool spots and few hard exudates (if hard exudate occurs around macula or fovea, it is called **macular star**).

My diagnosis is **hypertensive retinopathy**.

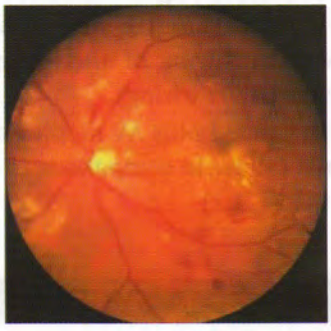
Presentation of Case No. 2

- As in Case 1 **plus** papilloedema.

My diagnosis is **hypertensive retinopathy** (malignant hypertension).



Flame-shaped haemorrhage, cotton wool spot, papilloedema



Flame-shaped haemorrhage, cotton wool spot, macular star, arteriolar straightening

Q: Why **not** this is diabetic retinopathy?

A: In diabetic retinopathy:

- Haemorrhage: usually dot and blot.
- No AV nipping.
- Hard exudate.

Q: What are the **causes** of AV nipping?

A: As follows:

- Hypertensive retinopathy (grade II).
- Atherosclerosis.

Q: What is **cotton-wool spot** and what are the **causes**?

A: It indicates area of retinal infarction or ischaemia. Its causes are:

- Hypertension.
- Occasionally DM.
- Central retinal vein occlusion.
- Central retinal artery occlusion.
- Severe anaemia.
- SLE (called cytoid body).
- Others include leukaemia, infective endocarditis (Roth spot), HIV infection.

Q: What is **malignant hypertension**? What does it **indicate**?

A: It means papilloedema with blood pressure (BP); mainly the diastolic > 130 mmHg with or without renal impairment. It indicates cerebral oedema.

Q: What is the **pathogenesis** of malignant hypertension?

A: Unknown, probable mechanisms are:

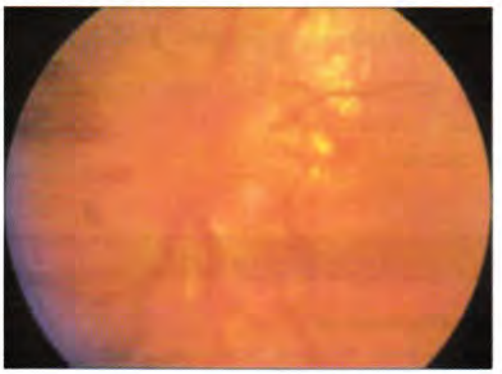
- Fibrinoid necrosis of the wall of small artery and arteriole, which results in end-organ damage.
- Dilatation of cerebral arterioles (due to auto-regulation), which may result in cerebral infarction or haemorrhage.

It may be reversible after treatment. In malignant hypertension, papilloedema may occur in the absence of haemorrhage and exudate.

Q: What are the **grades** of hypertensive retinopathy?

A: Four grades (Keith–Wagener–Barker classification):

- **Grade I:** Thickening of arterial wall, increase tortuosity, narrowing of arteriole and increased light reflex (silver wiring).
- **Grade II:** Grade **I plus** AV nipping and reduction of arterial calibre in comparison to vein (normal ratio of V:A = 3:2).
- **Grade III:** Grade **II plus** cotton-wool exudate and flame-shaped haemorrhage.
- **Grade IV:** Grade **III plus** papilloedema (Grades III and IV indicate malignant hypertension).



Grade IV retinopathy

Q: What are the ocular complications of hypertension?

A: Retinal vein occlusion and retinopathy.

Retinal Haemorrhage

Usual instructions are:

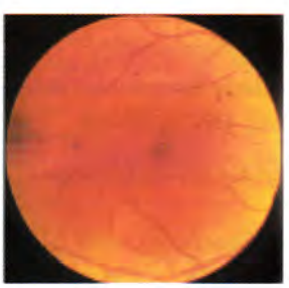
- Examine the fundus. What are your findings?

Presentation of the Case

- There are few haemorrhages (mention the location), some are flame shaped and some are irregular in outline.
- The fundus looks pale.

My **differential diagnoses** are (mention the causes of that patient according to age):

- Aplastic anaemia.
- Leukaemia.
- Thrombocytopaenia.
- Haemophilia.
- Christmas disease.
- Severe anaemia due to any cause.
- Anticoagulant drug therapy.



Retinal haemorrhage in diabetic retinopathy



Retinal and preretinal haemorrhage

Q: What are the **causes** of retinal haemorrhage?

A: As follows:

- Hypertension.
- Diabetes mellitus.
- Atherosclerosis.
- CRVO due to any cause.
- Subarachnoid haemorrhage (subhyaloid with crescentic-shaped or straight horizontal border).
- Raised intracranial pressure due to any cause.

Q: How to **treat** retinal haemorrhage?

A: Treatment of underlying cause.

Q: What is **Roth spot**? What are the **causes**?

A: Retinal haemorrhage with a white spot in the centre is called Roth spot. Its causes are:

- Infective endocarditis (due to autoimmune vasculitis).
- Leukaemia.
- SLE.
- Severe anaemia.



Roth spot



Roth spot with haemorrhage

Diabetic Retinopathy

Usual instructions are:

- Examine the fundus. What are your findings?

Presentation of Case No. 1

(Mention in which eye, right or left)

- There are microaneurysm of capillaries (mention the location).
- Few haemorrhages (dot and blot), which are small and round shaped.
- Also there are hard exudates (yellowish with clear margin).
- Disc is normal.

My diagnosis is **diabetic retinopathy**, simple background.



Dot and blot haemorrhage (soft exudate)



Dot and blot haemorrhage (hard exudate)

Q: Why this is **not** hypertensive retinopathy?

A: In hypertensive retinopathy, there will be:

- AV nipping.
- Soft or cotton-wool exudate.
- Flame-shaped haemorrhage.

Q: What is microaneurysm? What are the causes of microaneurysm of capillaries?

A: Microaneurysms are the out-pouching of capillary walls due to pericyte loss, appears as small red dots. It is the early sign of diabetic retinopathy. Causes are:

- Diabetes mellitus.
- Hypertension (usually in malignant hypertension).
- Atherosclerosis.
- Collagen diseases (SLE and polyarteritis nodosa, PAN).
- Hyperviscosity syndrome (macroglobulinaemia).
- Others include sickle cell anaemia, leukaemia, mycotic aneurysm and retinal vein occlusion.

N.B. Microaneurysm is always along the vessel wall, and it may be confused with haemorrhage. It is confirmed by fluorescence angiography.

Q: Why haemorrhage?

A: It is due to rupture of microaneurysm, resulting in dot and blot haemorrhage.

Q: What are **hard exudates**?

A: These are lipid and protein residues of serous leakage from the vessels, yellowish in colour and irregular in outline with sharply defined margin.

Q: In simple background retinopathy, what are the **symptoms** of the patient?

A: Usually asymptomatic, as the macula is spared.

Q: How to **treat** such a case?

A: As follows:

- Control of diabetes mellitus, stop smoking and control of hypertension (if any).
- Annual fundal examination.
- For leaking microaneurysm: Argon laser photocoagulation may be done.

N.B. Simple retinopathy is rare in young if DM < 10 years duration, but common if > 20 years duration. In older diabetes mellitus, early development may occur.

Presentation of a Case (Maculopathy): Case No. 2

- Findings as in Case 1 **plus**
- Haemorrhage and hard exudates encroaching upon the macula (maculopathy or macular oedema).

My diagnosis is **background diabetic retinopathy with maculopathy**.

Q: What are the **symptoms** of the patient?

A: Visual impairment, mainly central vision (reduction of visual acuity). Diabetic maculopathy is one of the common causes of loss of vision in patient with non-proliferative retinopathy.

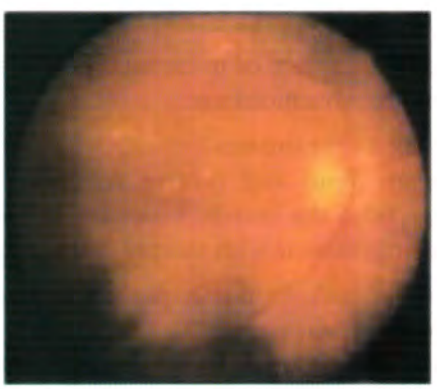
Q: In which **diabetes** it is common?

A: It is common in the elderly, and is of non-insulin-dependent diabetes mellitus (NIDDM).

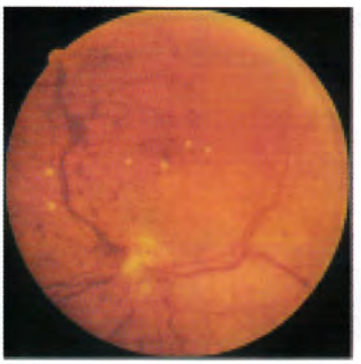
Q: How to **treat** such a case?

A: As follows:

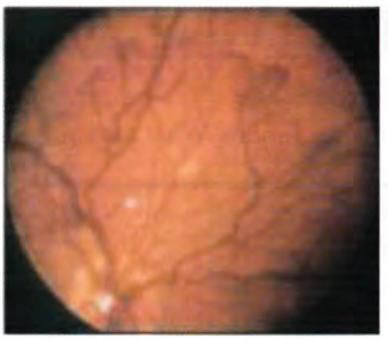
- Good control of diabetes mellitus.
- Photocoagulation may improve visual acuity in 50% cases.



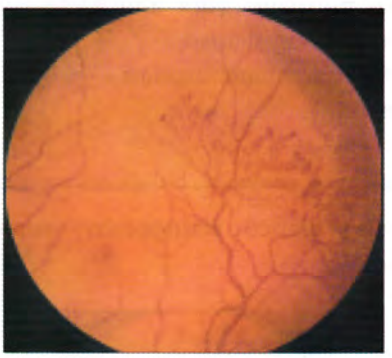
Maculopathy



Preproliferative retinopathy



Proliferative retinopathy (advanced stage, severe)



Proliferative retinopathy (early stage)

Presentation of Case No. 3

(Mention in which eye, right or left)

- As in case no. 2 **plus**
- Multiple large blot haemorrhages and cotton-wool spots.
- Venous dilatation, venous beading and venous loops are also present.

My diagnosis is **preproliferative diabetic retinopathy**.

Q: What are the features of **preproliferative** retinopathy?

A: As follows:

- Multiple cotton-wool spots (the earliest sign).
- Venous abnormality (irregular, beading, reduplication and loops).
- Multiple haemorrhage and intraretinal microvascular abnormality.

Q: How to **treat** preproliferative retinopathy?

A: As follows:

- Good control of DM.
- Photocoagulation in some cases.
- Regular follow-up should be done.

Presentation of a Case (Proliferative Type): Case No. 4

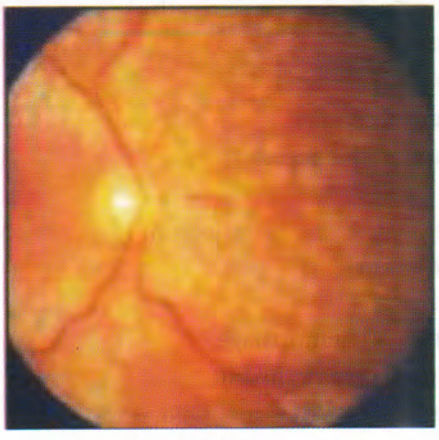
- Findings as in case no. 3 **plus**
- Venous dilatation, tortuosity and beading.
- There are some new vessel formations around the disc.
- There are few vitrious haemorrhage.

My diagnosis is **proliferative diabetic retinopathy**.

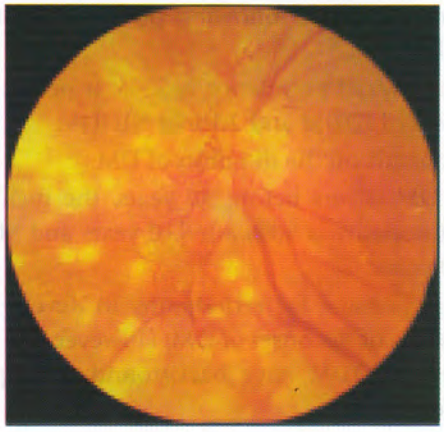
Presentation of Case No. 5

- As in case no. 4. **plus**
- There are multiple photocoagulation scars (appears like exudate, with areas of small brown or yellowish spot of variable size and shape).

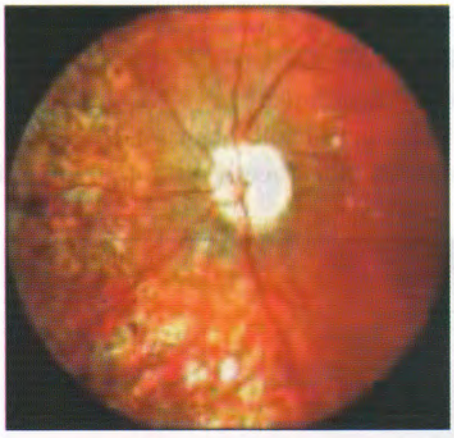
My diagnosis is **proliferative diabetic retinopathy, treated with photocoagulation**.



Panretinal photocoagulation



Retinal photocoagulation



Panretinal photocoagulation

Q: What are the **features of proliferative** retinopathy?

A: As follows:

- Exudative maculopathy.
- Preretinal haemorrhage.
- New vessels formation and fibrous proliferation.

Q: What are the **symptoms** of the patient in proliferative retinopathy?

A: As follows:

- Asymptomatic without macular involvement.
- Blurring of vision with macular involvement.

Q: What is the **treatment** of proliferative retinopathy?

A: As follows:

- Good control of DM.
- Photocoagulation.

Q: What is the **prognosis**?

A: Prognosis of proliferative retinopathy is variable if untreated. 50% may develop blindness within 5 years.

Q: In which **type of DM**, proliferative retinopathy is more common?

A: It is common in IDDM of long duration.

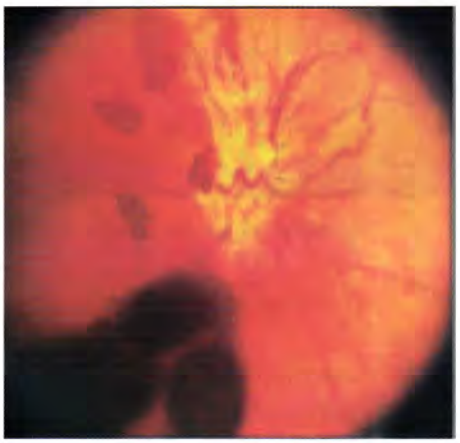
N.B. Remember the following points of retinopathy in DM:

- The overall prevalence is 25%. It occurs in 40% cases of IDDM and 20% of NIDDM.
- Depends on the duration of DM.
- If DM occurs before 30 years, the incidence of retinopathy is 50% after 10 years and 90% after 30 years.
- It is unusual for retinopathy to develop within 5 years of the onset of DM. However, 5% patients with NIDDM have background retinopathy at presentation.

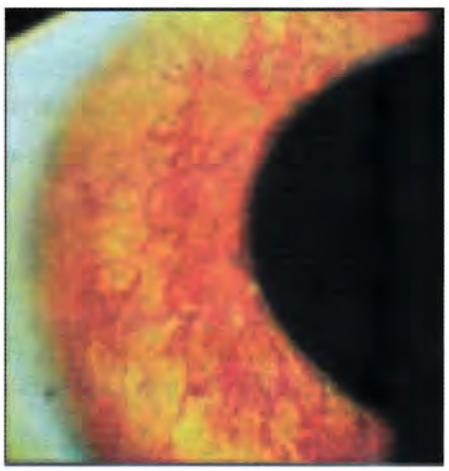
Q: What are the **complications** of proliferative retinopathy?

A: As follows:

- Vitreous haemorrhage.
- Retinal detachment.
- Glaucoma (rubeotic glaucoma).
- Rubeosis iridis (new vessel formation in iris).



Vitreous haemorrhage



Rubeosis iridis

Q: What are the **causes of retinal neovascularization**?

A: As follows:

- DM.
- Rarely malignant hypertension, sickle cell anaemia, sarcoidosis, hyperviscosity syndrome and Behcet syndrome.

Q: What is the **pathogenesis** of new vessel formation?

A: Unknown, probably there is production of angiogenic factors from the area of ischaemic retina. Recently, a substance called "vascular endothelial growth factor" (VEGF) has been isolated from ocular fluid, which is angiogenic.

These new vessels are very fragile and leaking, liable to rupture causing haemorrhage (intraretinal, preretinal or vitreous). Serous protein leakage from these vessels stimulates connective tissue reaction called retinitis proliferans. Later on, retinal detachment may occur.

Q: What are the eye problems in diabetes mellitus?

A: As follows:

- Diabetic retinopathy.
- Cataract.
- Central retinal vein occlusion.
- Glaucoma.
- Rubeosis iridis.
- Retinal artery occlusion.

Q: What is the cause of visual loss in diabetes mellitus?

A: As follows:

- Macular oedema.
- Proliferative retinopathy.
- Retinal detachment.

Q: What are the indications of laser photocoagulation therapy in diabetic retinopathy?

A: As follows:

- Macular oedema.
- Preproliferative.
- Proliferative retinopathy.

Q: What are the complications of laser photocoagulation therapy?

A: As follows:

- Vitrious haemorrhage.
- Retinal vein occlusion.
- Constriction of visual field.
- Headache.

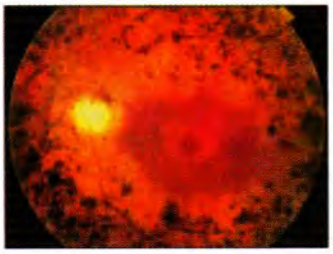
Retinitis Pigmentosa

Usual instructions are:

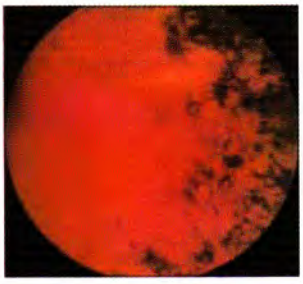
- Examine the fundus. What are your findings?

Presentation of a Case

- There are multiple areas of black pigmentation like bone corpuscles with variable size and shape, some in criss-cross pattern, at the periphery of fundus.
- Macula is normal, and the disc is also normal.
- No exudate or haemorrhage.



Retinitis pigmentosa (advanced stage, severe)



Retinitis pigmentosa (early stage)

My diagnosis is **retinitis pigmentosa**.

Q: What is the **differential diagnosis**?
A: Old choroidoretinitis.

Q: What is **retinitis pigmentosa**? What are the **features**?
A: It is a progressive degenerative disease of the retina with pigmentary epithelium in a bone spicule pattern.

- It starts in early childhood and affects both eyes.
- Inherited as X-linked, autosomal recessive or autosomal dominant.
- May occur sporadically as an isolated ocular disorder and also associated with other disease.
- Degeneration primarily affects the rods, and also may involve cones.
- Loss of vision by middle or advanced age. Visual acuity is normal initially, and patient becomes blind by 20–30 years.
- There may be constriction of peripheral field of vision and OA (consecutive).
- Cataract is a common complication causing further visual impairment.

Q: What are the **causes** of retinitis pigmentosa?
A: As follows:

- Isolated or congenital. Laurence–Moon–Biedl syndrome (features: dwarfism, polydactyly, obesity, hypogonadism and mental retardation).
- Hereditary ataxia (Friedreich ataxia).
- Refsum disease.
- Abetalipoproteinaemia.
- Usher disease.
- Alström syndrome.
- Familial neuropathies.

Q: What is the **common complaint** or **presentation** of retinitis pigmentosa?
A: Night blindness (due to reduction of rods at the periphery of retina).

Q: How to **treat**?
A: As follows:

- Regular and periodic check-up.
- Treatment of primary cause.

Ptosis

Usual instructions are:

- Look at the face. What else do you want to see?
- Examine the eyes.

(If there is obvious ptosis, is it bilateral or unilateral, complete or partial? Ask the patient to open the eyes, but the patient is unable.)

Presentation of a Case (Unilateral Ptosis of the IIIrd Nerve Palsy): Case No. 1

- There is complete ptosis in the right (or the left) side.



Unilateral ptosis – IIIrd nerve palsy (left)



Right-sided IIIrd nerve palsy

Q: What else do you want to see?

A: As follows (raise the upper eye lid):

- Divergent squint (eyeball is fixed in downward and outward position).
- Pupil (dilated and fixed, and no reaction to direct and consensual light).
- No movement of eyeball in upwards, downwards and medially.
- Loss of accommodation.
- May be diplopia (angulated, mention in which direction).

Q: What is your diagnosis?

A: IIIrd nerve palsy.

Q: What are the causes of unilateral ptosis?

A: As follows:

- Congenital.
- Traumatic.
- Senility.
- Complete IIIrd nerve palsy.
- Horner syndrome (partial ptosis). Myasthenia gravis (may cause unilateral or bilateral ptosis).
- Hysterical conversion reaction (HCR).

N.B. IIIrd nerve palsy may be partial; pupil may be spared. Occurs in DM and vasculitis, which causes infarction of the nerve. Parasympathetic fibres supplying the pupil remain intact and spare the pupil.

Q: Why ptosis and dilated pupil in the IIIrd nerve palsy?

A: As follows:

- Ptosis is due to paralysis of levator palpebrae superioris (supplied by IIIrd nerve).
- Dilated pupil is due to paralysis of the constrictor of pupil (supplied by IIIrd nerve).

(Dilator of pupil is supplied by sympathetic nerve, which when paralyzed, pupil is constricted as in Horner syndrome).

Q: What are the causes of IIIrd nerve lesion?

A: As follows:

1. Nuclear lesion (infarction, haemorrhage, neoplasm and multiple sclerosis).
2. Midbrain with CVA (Weber syndrome: ipsilateral IIIrd nerve palsy with contralateral hemiplegia due to thrombosis of a branch of posterior cerebral artery).
3. Unruptured aneurysm of posterior communicating artery (painful ophthalmoplegia).
4. Others:
 - Mononeuritis multiplex (DM, SLE, PAN, sarcoidosis, amyloidosis and leprosy).
 - Subacute meningitis (carcinomatous, lymphomatous, fungal, tuberculous and meningovascular syphilis).
 - Raised intracranial pressure (because the nerve has long and tortuous course, so likely to be compressed by any displacement of brain stem).
 - Ophthalmoplegic migraine and Guillain–Barré syndrome.

Q: What are the signs of IIIrd nerve lesion?

A: As follows:

- Ptosis (complete).
- External squint.
- Pupil: Dilated, no reaction to direct and consensual light.
- Inability to move the eye upwards, downwards and medially.
- Loss of accommodation reflex.

Q: What investigations do you suggest in IIIrd nerve palsy?

A: As follows:

- Blood sugar.
- FBC (erythrocyte sedimentation rate [ESR] is high in vasculitis).
- CT or MRI of brain.
- Occasionally, cerebral arteriography (if aneurysm is suspected).

Presentation of a Case (Bilateral Ptosis): Case No. 2

- There is bilateral ptosis. Eye movement is normal.
- Pupil: Normal in size and shape, and reacts to direct and consensual light.
- Accommodation is normal.

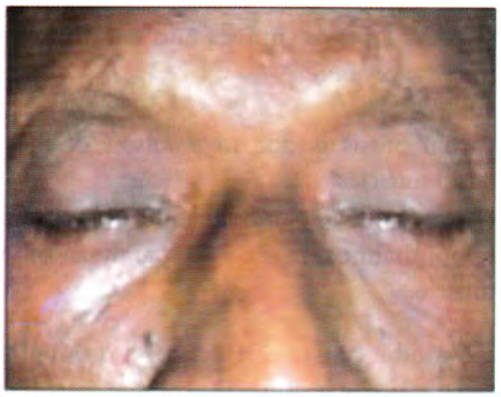
(See frontal baldness, wasting of temporalis and myotonia in myotonia dystrophica.)



Bilateral ptosis (congenital)



Bilateral ptosis (myasthenia gravis)



Bilateral ptosis (senile)



Bilateral ptosis (ocular myopathy)

Q: What are the causes of bilateral ptosis?

A: As follows:

- Myasthenia gravis. Tabes dorsalis (bilateral ptosis with frontalis overaction, Argyll Robertson [AR] pupil, OA and dorsal column lesion). Myopathy (myotonia dystrophica and fascioscapulohumeral myopathy).
- Ocular and oculopharyngeal myopathy.
- Congenital (rare). Bilateral Horner syndrome (rare, may occur in syringomyelia).

N.B. If the patient has myopathy, no wrinkling of forehead. In other cases, there is overaction of frontalis with wrinkling of forehead.

Presentation of a Case (Ocular Myopathy): Case No. 3

- There is bilateral ptosis, no compensatory wrinkling of forehead (may be wasting of muscles of face and neck).
- No movement of eyeball in any direction (complete ophthalmoplegia).
- Pupil is normal in size and shape, reacts to direct and consensual light.
- Accommodation is normal.

My diagnosis is **ocular myopathy** or **oculopharyngeal myopathy**.

Q: What is ocular myopathy?

A: It is a hereditary disorder, inherited as autosomal dominant (AD) or sporadic, common in young, characterized by bilateral ptosis with complete ophthalmoplegia. It may be due to absence of soft tissue in eyelid and periorbital region, also causes mild facial and neck weakness.

Q: What is oculopharyngeal myopathy?

A: Like ocular with dysphagia due to cricopharyngeal achalasia, common in the elderly.

Presentation of a Case (Myotonic Dystrophy): Case No. 4

- There is bilateral ptosis with frontal baldness, wasting of temporalis, masseter and sternomastoid.
- Face is long, lean, sad and expressionless.

My diagnosis is **myotonia dystrophica** (see page 356).

N.B. During examination for ptosis, remember the following points:

- If complete ptosis with divergent squint and dilated pupil, IIIrd nerve palsy.
- Partial ptosis with apparent enophthalmos and constricted pupil, Horner syndrome.
- Absence of movement in any direction, ocular or oculopharyngeal myopathy.
- Frontal baldness and temporal wasting, myotonic dystrophy.

Horner Syndrome

Usual instructions are:

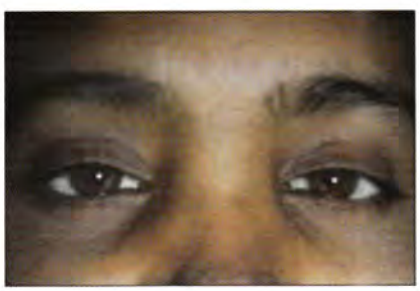
- Examine the eye of this patient.
- Look at the eyes. What are your findings?

Presentation of a Case (Horner Syndrome): Case No. 1

(Mention in which eye)

- There is partial ptosis with enophthalmos (eyeball looks shrunken and inwards).
- Pupil constricted (miosis), and reacts to direct and consensual light.
- Movement of the eyeball is normal.

My diagnosis is **Horner syndrome** (right or left sided).



Horner syndrome (bilateral)



Horner syndrome (left)

Q: What else do you want to see in this patient?

A: As follows:

- Neck: Lymph nodes, scar, thyromegaly, aneurysm (carotid and aortic).
- Chest: Apical signs (Pancoast tumour).
- Hands: Clubbing, nicotine stain, wasting of small muscles of hands and pain.
- Evidence of syringomyelia (dissociated sensory loss).
- Evidence of lateral medullary syndrome.
- Absence of sweating (affected side of face, whole upper limb and upper part of trunk).

Q: What is Horner syndrome?

A: It is a syndrome due to lesion in the sympathetic pathway characterized by:

- Partial ptosis.
- Miosis (pupillary constriction), reacts to direct and consensual light.
- Enophthalmos.
- Anhydrosis (absence of sweating in affected side of face, whole upper limb and upper part of trunk).

Q: Why partial ptosis, miosis and enophthalmos in Horner syndrome?

A: As follows:

- Partial ptosis is due to paralysis of the upper tarsal muscles.
- Miosis is due to paralysis of the dilator of pupil.
- Enophthalmos is due to paralysis of Muller muscle.

Q: What are the causes of Horner syndrome (according to the site of lesion)?

A: As follows:

1. T_1 lesion:
 - Pancoast tumour.
 - Trauma to brachial plexus.
 - Cervical rib.
2. Neck (sympathetic lesion):
 - Trauma.
 - Neck surgery.
 - Cervical sympathectomy.
 - Lymphoma.
 - Thyroid carcinoma.
3. Brain stem lesion:
 - Vascular (lateral medullary syndrome).
 - Multiple sclerosis.
4. Cervical cord lesion (bilateral Horner syndrome may occur):
 - Syringomyelia.
 - Spinal cord tumour (glioma and ependymoma).
5. Migraine (temporary Horner syndrome may occur).

Q: What **investigations** should be done in Horner syndrome?

A: As follows:

- Chest x-ray.
- X-ray of cervical spine.
- CT scan or MRI of brain.
- Other investigations, according to suspicion of causes.

Q: Discuss the **cervical sympathetic pathway**.

A: It originates from the sympathetic nucleus in hypothalamus and passes through the brain stem to the lateral horn of C_8 and T_1 segment of spinal cord. From there, preganglionic fibres emerge and pass to sympathetic ganglia (usually superior cervical ganglia). Then the post-ganglionic fibres pass in the carotid sheath with internal carotid artery (ICA), enter the skull along with it and in the cavernous sinus, and join with the ophthalmic division of the Vth nerve. Then it enters into the orbit, via short ciliary nerve, and supply the dilator pupillae, Muller muscle and sweat gland on the side of face.

Argyll Robertson Pupil (AR Pupil)

Usual instructions are:

- Examine the eye of this patient.
- Look at the eyes. What are your findings?

Presentation of a Case

(AR pupil is always bilateral)

- Both the pupils are irregular, small and unequal.
- There is loss of light reflex (both direct and consensual).
- Accommodation reflex is normal.
- Iris is patchy atrophy and depigmentation.

My diagnosis is **AR pupil**.



AR pupil

Q: What are the **causes** of AR pupil?

A: As follows:

- Neurosyphilis, as in tabes dorsalis, and general paralysis of the insane (GPI), the commonest cause.
- DM.

Q: What are the **features** of AR pupil?

A: As follows:

- Pupil is small, irregular and unequal.
- Loss of light reflex, but persistence of accommodation reflex.
- Impaired response to mydriatic drug.
- Iris shows patchy atrophy and depigmentation.

Q: What is **site of lesion** of AR pupil?

A: Tectum of midbrain proximal to oculomotor nucleus, around aqueduct of sylvius.

Q: The patient has AR pupil. What else do you want to see?

A: Other features of tabes dorsalis need to be noted:

- Wrinkling of forehead with bilateral ptosis (due to compensatory overaction of frontalis).
- Flaccid paraplegia.
- Loss of knee and ankle jerks, plantar is flexor (but in taboparesis, may be extensor).
- Posterior column lesion (loss of vibration and position sense).
- Loss of deep pain in Achilles tendon.

- Hypotonia.
- Bladder sensation is lost (urinary retention and overflow incontinence).
- Gait may be stamping or steppage gait.
- Romberg sign is positive.
- Charcot joints.
- Fundoscopy shows OA.

Q: What is the **lesion in heart linked** with AR pupil?

A: Aortic regurgitation.

Different Types of Pupil

Q: What are the causes of **constricted pupil (miosis)**?

A: As follows:

- Horner syndrome.
- AR pupil.
- Pontine haemorrhage.
- Senility (pupil in old age tends to be small, and may be irregular).
- Morphine.
- Miotic drugs (pilocarpine and physostigmine).
- Poisoning (organophosphorous, opium and trichloroethanol).

Q: What are the causes of **dilated pupil (mydriasis)**?

A: As follows:

- IIIrd nerve palsy.
- Holmes–Adie pupil.
- Optic nerve lesion (optic neuritis or retrobulbar neuritis).
- Mydriatic drugs (atropine and homatropine).
- Other drugs (tricyclic antidepressant, belladonna and amphetamine).
- Datura poisoning.
- Fixed dilated pupil (occurs in brain death, also in deep coma).

Q: What are the causes of **unequal pupil (anisocoria)**?

A: As follows:

- Physiological anisocoria in normal eye (20%).
- Iritis.
- Syphilis.
- Holmes–Adie pupil.
- Mydriatic drug in one eye.
- Blindness or amblyopia in one eye (pupil is large in affected eye).
- Cerebrovascular accident.

Q: What are the causes of **absent light reflex**, but **present accommodation reflex**?

A: As follows:

- AR pupil.
- Midbrain lesion.
- Ciliary ganglion lesion.

Q: What are the causes of **absent accommodation reflex**, but **normal light reflex**?

A: As follows:

- Cortical lesion (cortical blindness).
- Parkinson disease by encephalitis lethargica.

(Parkinson disease due to encephalitis lethargica, the pupils react to light, but not to accommodation, called **reverse** AR pupil).

Q: What is the **afferent** and **efferent** pathway of light reflex?

A: Afferent is through optic nerve and efferent is through the IIIrd cranial nerve.

Q: What is **Marcus–Gunn** phenomenon or pupil?

A: In this disorder, direct reflex is brisk on exposure to light. However, when light is alternately focused from one eye to other, the pupil on the affected side dilates slowly, when exposed to light. Found in optic neuritis.

The mechanism is as follows:

- When light is focused on healthy eye, a rapid pupillary constriction occurs in both eyes. When light is focused again on the affected eye, the eye fails to transmit the message to continue the constriction as quickly as normal. As a result, pupils have time to recover and dilate, despite the light shining on abnormal eye.

N.B. Read the following points in relation to pupil of unconscious patients:

- One pupil is dilated, fixed to light: Indicates herniation of uncus of temporal lobe (coning) and compression of IIIrd nerve.
- Pinpoint fixed pupil: Indicates pontine haemorrhage.
- Midpoint and slightly dilated pupil indicates damage to the midbrain with interruption of pupillary light reflex.
- Midpoint pupil that reacts to light indicates coma of metabolic origin and central nervous system (CNS) depressant drugs.
- Fixed dilated pupil (bilateral): Indicates brain death and deep coma.

Holmes–Adie Pupil

Usual instructions are:

- Examine the eye of this patient.
- Look at the eyes. What are your findings?

Presentation of a Case

- The pupil of right (or left) eye is dilated than other, regular (or circular).
- It does not react to light immediately, but when light is focused for a long time, it constricts slowly.
- Eye movements: Normal, no diplopia.

My diagnosis is **Holmes–Adie pupil**.



Holmes–Adie pupil (dilated right pupil)

Q: What else do you want to examine?
A: Tendon jerk (knee and ankle) on the same side, and both may be lost.

It is then called **Holmes–Adie syndrome**.

Q: What is Holmes–Adie pupil?
A: It is an abnormality characterized by absent or delayed pupillary constriction to light or accommodation. If exposed to light for prolonged period, pupil may constrict slowly. If then exposed to dark for long time, the pupil dilates slowly. During accommodation, after some delay, abnormal pupil constricts slowly, may be smaller than normal.

It is also called **myotonic** pupil, which is a benign condition, common in young women, usually unilateral (80%), and rarely bilateral. Hence, pupil appears unequal. It may be associated with loss of knee and ankle jerk on the same side. Its cause is not known.

Q: What is the site of lesion?
A: Ciliary ganglia (due to parasympathetic denervation).

Q: What is the significance of Holmes–Adie pupil?
A: It is a benign condition, should not be confused with AR pupil.

Q: What are the differences between AR pupil and Holmes–Adie pupil?
A: As follows:

AR pupil	Holmes–Adie pupil
Bilateral	Usually unilateral
Pupil: small, irregular and unequal	Regular, one pupil dilated
Loss of light reflex, but persistence of accommodation reflex	Slow reaction to light and accommodation
Impaired response to mydriatic	Normal response to mydriatic
Occurs in neurosyphilis	Unknown cause (benign condition)

Exophthalmos

Usual instructions are:

- Look at the face. What are your findings? What else do you want to examine?
- Examine the eyes.

Proceed as follows:

1. Look at the eyes from front, look and comment about sclera that is visible between the upper eyelid and the upper limbus of cornea. Observe for any swelling of eyelids, congestion of sclera, chemosis (oedema of conjunctiva), corneal ulceration and thyroid stare (a frightened expression).
2. Look at the eyes from behind to confirm proptosis (eyeball may be visible above the supraorbital ridge), and may require to place a paper between the supraorbital ridge and maxillary prominence (note the space between this).
3. If obvious exophthalmos, note the following points:
 - **Lid retraction** (by inspection, ask to look straight): The upper eyelid is retracted and sclera above the upper margin of corneal limbus is visible (normally one-third of the cornea is covered by the upper eyelid).

- **Lid lag** (ask the patient to follow your finger down): The upper eyelid fails to follow the finger (called **von Graefe sign**).
- Ask the patient to **wrinkle** the forehead (may be absent, called **Joffroy sign**).
- See the movement of the eyeball both horizontally and vertically (if movement is absent with exophthalmos, it is called **exophthalmic ophthalmoplegia**).
- During movement: Ask about **diplopia**.
- Test for **convergence** (impaired convergence is called **Möbius sign**).

4. Now examine the following points:
 - Signs of thyrotoxicosis (warm sweaty hands, tremor and tachycardia).
 - Signs of hypothyroidism (puffy face, baggy eyelid and loss of outer one-third of the eyebrows, coarse dry skin, non-pitting oedema and slow relaxation of ankle jerk).
 - Examine the thyroid gland (diffuse enlargement in Graves disease).

Presentation of a Case (Bilateral or Unilateral Exophthalmos)

- There is bilateral (or unilateral) exophthalmos (as evidenced by sclera above, the upper limbus is visible, and more marked on right or left).
- Eyelids are swollen; there is chemosis, redness and congestion of conjunctival vessels, and corneal ulceration. Eye movement is impaired of the right (or left) eye, (mention in which direction), this indicates ophthalmoplegia.
- There is diplopia on looking (mention in which direction).
- Impaired convergence (Möbius sign).
- Mention about lid lag, lid retraction and wrinkling of forehead (if any).

My diagnosis is **Graves disease**.



Bilateral exophthalmos (Graves disease)

N.B. For details, see page 264.

Q: What are the causes of exophthalmos?

A: As follows:

In **unilateral exophthalmos**, the causes are:

1. Graves disease (the commonest cause).
2. Orbital cellulitis.
3. Retro-orbital deposition found in:
 - Lymphoma.
 - Leukaemia.
 - Secondary deposit.
 - Hydatid cyst.
4. Tumours of the orbit:
 - Neurofibroma.
 - Sphenoidal ridge meningioma.
 - Osteoma.
 - Glioma (from optic nerve sheath).
 - Dermoid.

In **bilateral exophthalmos**, the causes are:

1. Graves disease (the commonest cause).
2. Cavernous sinus thrombosis.
3. Caroticocavernous fistula.
4. Others:
 - Hand–Schuller–Christian disease.
 - Craniostenosis.
 - Hypertelorism.
 - Apparently in severe myopia (eye is longer than normal).
 - Bilateral retro-orbital deposition (lymphoma and leukaemia).



Bilateral exophthalmos



Unilateral exophthalmos (right)

Q: What **investigations** do you suggest?

A: As follows:

- Thyroid function tests (for Graves disease) (See chapter on Endocrinology).
- Orbital ultrasonogram (USG).
- CT scan of orbit (enlargement of extraocular muscles, compression in optic nerve and proptosis).

Q: What is the **difference** between proptosis and exophthalmos?

A: It is synonymous; it means protrusion of the eyeball (according to some authority: If unilateral, it is called proptosis and if bilateral it is called exophthalmos). It is assessed by Hertel exophthalmometer (normally <20 mm).

Read the following topics carefully:

- ***Cavernous sinus thrombosis:*** Usually follows infection of nose, orbit or face. The patient is very toxic, with high temperature. Eyeballs are very painful and congested. Urgent treatment is necessary.
- ***Caroticocavernous fistula:*** There is pulsating exophthalmos and conjunctival congestion. A bruit is heard over the orbit, the intensity of which may be reduced by pressing over the carotid artery. Caroticocavernous fistula is due to rupture of infraclinoid part of the ICA to the cavernous sinus, mostly due to trauma or spontaneous. This may require neurosurgical intervention. In 10% cases, there may be small fistula, which resolves spontaneously.

Nystagmus

Usual instructions are:

- Examine the eyes. Or, examine the movement of eye. What are your findings?

Proceed as follows:

1. Ask the patient to sit, look straight in front and see whether nystagmus is present or not:
 - If present in central gaze, likely to be ocular nystagmus (fixation nystagmus).
 - If absent, then see in lateral gaze, called gaze nystagmus.
2. Now see any nystagmus by the movement of eyeball (horizontal and vertical):
 - Keep your finger straight in front of the eye (not below), 2–3 feet from the patient.
 - Move the finger laterally, patient should follow the finger up to 30° to the left and the right and keep your finger for 5 seconds (a guide of 30°: limbus and caruncle meet in adducting eye).
 - Do not move beyond 45° from central, and beyond that nystagmus may be physiological.
3. Observe, whether it is horizontal, vertical or rotatory.
4. Whether it is jerky or pendular and faster component in which direction.
5. During movement, observe whether nystagmus is present in abducting eye; at the same time, observe the failure of adduction of other eye (called **internuclear** ophthalmoplegia, which is also called **ataxic nystagmus**).

Presentation of a Case (Jerky Nystagmus): Case No. 1

- There is nystagmus in the right (or left) eye on lateral movement, faster component towards the right (or the left) side (horizontal, jerky nystagmus).
- No other abnormality in eye movement.
- Diplopia is absent.

My diagnosis is **horizontal, jerky nystagmus**.

Q: What do you think is the **cause** in this case?

A: May be cerebellar lesion (on affected side) or vestibular lesion (on contralateral side).

Q: What **else** do you want to examine?

A: As follows:

- Cerebellar signs (see chapter on Neurology).
- History of vertigo, deafness and tinnitus (suggests vestibular nystagmus).
- History of drugs, namely phenytoin and other anticonvulsants, barbiturates, alcohol, and benzodiazepines (all these may cause nystagmus).
- Nystagmus may present by movement of head to one side (positional nystagmus, and is found in benign positional vertigo).

Q: What is the **cause** of vertical nystagmus?

A: Due to brain stem lesion, causes are:

- Nystagmus on downward gaze: Lesion in foramen magnum (involving medulla).
- Nystagmus on upward gaze: Lesion on the floor of fourth ventricle (involving midbrain).

Q: What are the sites of lesion that produce nystagmus?

A: As follows:

- Cerebellar lesion.
- Vestibular lesion (central and peripheral).
- Brain stem.

Presentation of a Case (Internuclear Ophthalmoplegia): Case No. 2

- On lateral movement, there is nystagmus in the abducting eye and failure of adduction of other eye (dissociation of movement of other eye).
- On covering the abducting eye, adduction of other eye is normal.
- No other abnormality.

My diagnosis is **internuclear ophthalmoplegia** (ataxic or dissociated nystagmus).

Q: What is the site of lesion?

A: In medial longitudinal fasciculus (MLF) in the brain stem. MLF connects the VIth nerve nucleus on one side to the IIIrd nerve nucleus, which is on the opposite side of brain stem. The causes are:

- Multiple sclerosis (the commonest cause).
- Pontine glioma.
- Vascular cause (CVA).
- Wernicke encephalopathy (also there is ocular palsy, loss of pupillary reflex, ataxia and Korsakoff psychosis).
- Encephalitis.
- Phenytoin toxicity.

Read the following topics carefully:

Q: What is nystagmus?

A: It is the involuntary, rhythmical and oscillatory movement of the eyes due to inability to maintain the posture of eyes, owing to the lack of balance of the opposing ocular muscles. It is defined by the direction of fast phase and is exaggerated on gaze to that side. Nystagmus must be sustained for more than a few beats to be significant. Nystagmus may be jerky or phasic, pendular or ataxic (internuclear ophthalmoplegia).

Q: What are the types of nystagmus?

A: As follows:

1. According to the direction:
 - Horizontal.
 - Vertical.
 - Rotatory.
2. According to the site of lesion:
 - Cerebellar nystagmus (towards the site of lesion).
 - Vestibular nystagmus (away from the site of lesion).
 - Brain stem lesion (usually vertical nystagmus, and may be in other direction).
3. Others:
 - Positional nystagmus (associated with benign positional vertigo).
 - Ocular or fixation nystagmus (usually pendular type).
 - Optokinetic.
 - See-saw nystagmus.

Q: What is jerky nystagmus?

A: Jerky or phasic nystagmus is characterized by eye movement faster in one direction than other. Usually seen in horizontal direction, elicited on lateral gaze in one or both directions.

The causes are cerebellar lesion, vestibular lesion or lesions of their connection in the brain stem.

Q: What is pendular nystagmus?

A: In this type, oscillations are equal in speed and amplitude in both directions of the eye movement. It is usually seen in central gaze.

The cause is poor visual acuity (in severe refractive error or macular disease), usually congenital and asymptomatic.

Q: What is ataxic nystagmus?

A: In this type, on looking to one side, nystagmus is present in the abducting eye and there is failure of adduction of the other eye. It is also called "dissociated nystagmus" and is present in internuclear ophthalmoplegia.

Q: What are the causes of horizontal nystagmus?

A: As follows:

1. Cerebellar.
2. Vestibular nystagmus.
3. Brain stem lesion.
4. Others:
 - Ocular or fixation nystagmus (usually pendular type).
 - Optokinetic.
 - In normal person, in extreme lateral gaze.

Q: What are the causes of **vertical nystagmus**?

A: As follows:

- Brain stem lesion up-beating (midbrain lesion) and down-beating (medulla associated with foramen magnum lesion).
- Rarely, ocular nystagmus.

Q: What are the causes of **vestibular nystagmus**?

A: Vestibular nystagmus is usually horizontal or rotatory, and not vertical. It is of two types: peripheral and central.

1. Peripheral: Lesion in labyrinth or vestibular nerve. Fast component of nystagmus is contralateral to the site of lesion, may be associated with cochlear lesion. Its causes are:
 - Labyrinthitis (may be viral).
 - Meniere disease.
 - Acoustic neuroma.
 - Head injury.
 - Middle ear disease.
 - Vestibular neuronitis (presents with acute vertigo, tinnitus and deafness).
2. Central: Lesion is in vestibular nuclei. Its causes are:
 - Cerebrovascular accident.
 - Multiple sclerosis.
 - Neoplasm.
 - Alcohol.
 - Anticonvulsant drugs.

Q: What is **optokinetic** nystagmus?

A: It occurs when the patient follows a rapidly moving scene (as during travelling in a train, eye remains fixed to a telegraph pole). It is a normal phenomenon.

Q: What is **see-saw** nystagmus?

A: In this condition, one eye raises and turns in and the other eye falls and turns out. It is due to parasellar tumour.

Q: What is **positional** nystagmus?

A: In this condition, nystagmus is present in certain position and rapid movement of the head.

- It can be detected by **Hallpike test**, in which the patient should lie on the back, support the head and allow to fall below horizontal plane and turn to one side.
- After a few seconds, rotatory nystagmus and vertigo develop. If the position is maintained, fatigue occurs after 10–20 seconds, nystagmus and vertigo disappear.
- If the test is repeated immediately, there is little response (adaptation). It is usually associated with benign positional vertigo.

Causes: Calcific degeneration of utricle and saccule of the inner ear causes small particles to fall on to the cupola of semicircular canal during the movement of head.

Subhyaloid Haemorrhage

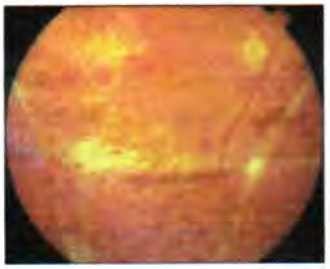
Usual instruction:

- Perform fundoscopy.

Presentation of a Case

- There is haemorrhage with crescentic shape or upward concavity in the right eye.
- Other part of the retina is normal (there may be bleeding spots in the retina).

My diagnosis is **subhyaloid haemorrhage**.



Subhyaloid haemorrhage

Q: What are the **typical findings** in subhyaloid haemorrhage?

A: Sharply demarcated preretinal (subhyaloid) haemorrhage with a fluid level (crescentic or upward concavity).

If the patient is in supine position, then the fluid level is not seen. Retinal haemorrhage and mild papilloedema may be seen. The haemorrhage may extend into the vitreous humour, which is called Terson syndrome.

Q: What is the **presentation** of subhyaloid haemorrhage?

A: The patient presents with sudden painless loss of vision. There may be blurring or floaters or black spots with or without flashing lights. There may be features of subarachnoid haemorrhage.

Q: What are the causes of **vitreous haemorrhage**?

A: As follows:

- SAH.
- Diabetes mellitus.
- Hypertension.
- Blood dyscrasia.
- Trauma.

Q: What is the cause of subhyaloid haemorrhage?

A: Subarachnoid haemorrhage is the commonest cause (subhyaloid haemorrhage is pathognomonic of SAH).

Q: What are the features of SAH?

A: As follows:

- Sudden severe headache, usually occipital (thunder-clap headache or struck by a hammer).
- Nausea, vomiting.
- Loss of consciousness.
- Neck rigidity.
- Kernig sign may be positive.

Q: What are the causes of SAH?

A: As follows:

- Rupture of berry aneurysm.
- Arteriovenous malformation (AVM).

Q: What investigations do you suggest for SAH?

A: As follows:

- CT scan of head (preferable over MRI).
- CT angiogram may be done if needed.
- Lumbar puncture and CSF study may be done.
- Cerebral angiography will be needed later to find out the source.

Q: What are the findings in CSF?

A: As follows:

- High pressure.
- Frankly haemorrhagic fluid.
- Xanthochromia (when kept for some hours).

Q: How will you differentiate the CSF finding of SAH from trauma?

A: In case of trauma, the initial sample is mixed with blood, but subsequent samples show clear fluid or less blood. But in SAH, all the test tubes have fluid mixed with blood. Xanthochromia is absent in traumatic blood.

N.B. Remember the following points regarding SAH:

- More common in women.
- Immediate mortality is 30%.
- Chance of recurrence is 40% in 4 weeks and 3% annually.
- Berry aneurysm arises from bifurcation of circle of Willis.
- If the patient with SAH deteriorates, it indicates either rebleeding or cerebral infarct due to reflex vasospasm of the cerebral vessels (which can be prevented by using nimodipine).

Choroidoretinitis

Usual instruction:

- Perform fundoscopy.

Presentation of a Case

- There are multiple pigmented patches with whitish or greyish areas within these, seen on the upper and temporal side of the right eye.
- There is no haemorrhage, but exudates are present.
- Vessels are normal.

Diagnosis is **choroidoretinitis**.



Chorioretinitis in toxoplasmosis

Q: What are the causes of choroidoretinitis?

A: As follows:

- Toxoplasmosis.
- Tuberculosis.
- Sarcoidosis.
- Syphilis.
- Toxocariasis.
- Behcet disease.
- CMV infection.
- HIV (AIDS).

Q: Why there is pigmentation?

A: It indicates exposed sclera due to old choroiditis, causing atrophy of the choroidoretina.

Q: What are the presentations with choroidoretinitis?

A: Patient may complain of reduced vision, floaters and redness of eye. Features of primary disease may be present.

Q: What are the typical findings of CMV retinitis?

A: There may be haemorrhage, oedema and exudate. Typically, it looks like cottage cheese and ketchup.

Q: How would you **treat** CMV retinitis?
A: Ganciclovir or foscarnet (intravenous).

Q: What are the **other causes** of pigmentation in retina?
A: As follows:

- Photocoagulation.
- Retinitis pigmentosa.
- Malignant melanoma.
- Racial (tigroid fundus).

Q: What is the **prognosis**?
A: Poor, if fovea is involved. Also depends on aetiology.

Q: What are the retinal changes in AIDS?
A: As follows:

- Due to CMV (see above).
- Due to HIV—cotton wool spots.

Retinal Detachment

Usual instruction:

- Perform fundoscopy.

Presentation of a Case

- The retina is opaque and grey in the left eye (no pink colour).
- There is ballooning detachment with numerous folds (indicates large collection of subretinal fluid).

My diagnosis is **retinal detachment**.



Retinal detachment

Q: What are the **causes**?
A: As follows:

- Uncontrolled diabetes mellitus.
- Retinal surgery (loss of vitreous following cataract surgery).
- Trauma (perforating eye injury).
- Chronic inflammation.
- Posterior vitreous detachment.
- Severe myopia.
- Systemic disease: Hypertension, toxaemia of pregnancy, chronic glomerulonephritis, retinal venous occlusive disease, retinal vasculitis.

Q: What is the **presentation**?
A: As follows:

- Flashes of bright light (photopsia) in the peripheral part of vision.
- Floaters in the eye.
- Feeling of heaviness in the eye.
- Blurring of vision.
- Blindness or shadow starting peripherally and progressing centrally. The patient typically describes a curtain or veil being drawn over the visual field.
- Loss of central vision.

Q: What is the **mechanism** of retinal detachment?
A: Separation within the retina between the photoreceptors and retinal pigmented epithelium, characterized by collection of fluid and blood in this space.

Bitemporal Hemianopia

Usual instruction:

- Examine the field of vision. Or, examine the optic nerve.
- Look at the patient (acromegaly). With this diagnosis what would you like to examine in the eyes.

Presentation of a Case

- There is loss of vision on the temporal side in both eyes.
- Central vision is intact.

Diagnosis is **bitemporal hemianopia**.

Q: What is the site of lesion?

A: Centre of the optic chiasma, damaging the fibers from nasal half of retina, as they decussate at chiasma. This will result in loss of both temporal half of visual field.

Q: What are the causes?

A: As follows:

- Pituitary tumour.
- Craniopharyngioma.
- Sarcoidosis.
- Suprasellar meningioma.

Q: What are the presentations?

A: May not be any complaint, but sometimes diplopia. Patient may complain of repeated collision on the sides with another person or door etc.

Q: What investigations do you suggest?

A: As follows:

- Perimetry.
- X-ray skull.
- MRI of brain.
- Pituitary hormone assay.

Miscellaneous

Corneal Arcus



Corneal arcus

It is a crescentic whitish opacity, like a line near the periphery of cornea. Usually, starts at lower part, ultimately completes the circle.

- Corneal arcus indicates annular infiltration of lipid in the peripheral rim of cornea.
- A normal finding in the elderly (arcus senilis).
- Sometimes, it is associated with hypercholesterolaemia, especially in young patients (arcus juvenilis). May also be present in type IV hyperlipoproteinaemia.

Pingueculae

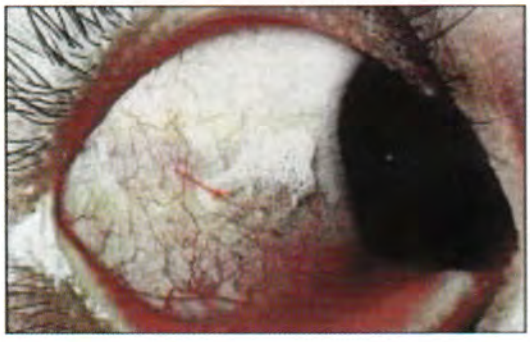


Pingueculae

Yellowish thickening of conjunctiva, may be on either side of cornea, progresses towards cornea, but does not cover it. It is due to the hyaline degeneration of elastic tissue. Its causes are:

- In the elderly, exposure to dust and fume.
- Gaucher disease.

Bitot Spot





Bitot spot



Keratomalacia

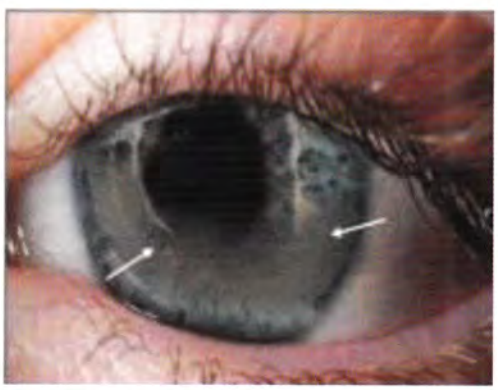
These are white plaques of desquamated, thick conjunctival epithelium. These are triangular in shape, usually found in young patients, due to vitamin A deficiency. Sometimes, may occur due to exposure to dust and glare.

Q: What are the eye problems that occur due to vitamin A deficiency?

A: As follows:

1. Night blindness.
2. Xerophthalmia:
 - Initially, xerosis conjunctivae (dry, thick, there is pigmented bulbar conjunctiva associated with smoky appearance), then Bitot spot.
 - Later, when dryness spreads over the cornea, it is dull, hazy and lacks lustre due to keratinization—called xerophthalmia.
3. Keratomalacia: Corneal opacity, ulcer and dissolution leading to blindness.
4. Treated with vitamin A, otherwise blindness may occur.

Band Keratopathy



Band keratopathy

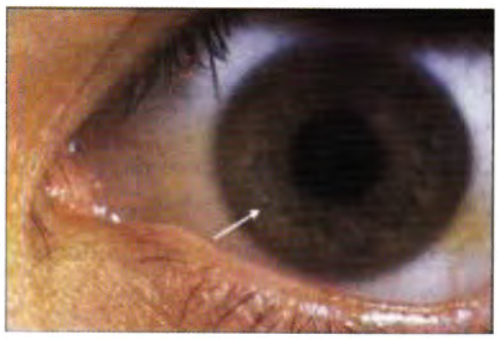
It is the subepithelial deposition of calcium salt in the cornea with a clear zone separated from limbus. Its causes are:

- Hypercalcaemia due to any cause.
- Iridocyclitis in children.
- Idiopathic in children.
- Phthisis bulbi.

Treatment:

- Chelating agents, such as sodium versenate, are helpful.

Kayser–Fleischer Ring



Kayser–Fleischer ring

It is a greenish-brown discolouration at the corneal margin, usually appears first at the upper periphery, and then encircles the whole cornea. It is due to the deposition of copper in Descemet membrane of cornea. It may not be seen by naked eye, and requires slit-lamp examination.

Presence of KF ring is pathognomonic of Wilson disease. Found in adult (60%), almost always present in neurological Wilson disease. It may be absent or less in young children. It is rarely found in primary biliary cirrhosis. KF ring disappears with treatment.

Blue Sclera



Blue sclera

Its causes are:

- Isolated.
- Osteogenesis imperfecta.
- Marfan syndrome.

- Homocystinuria.
- Ehlers–Danlos syndrome.
- Pseudoxanthoma elasticum.

Q: What are the causes of sudden blindness?

A: Sudden blindness may be in one eye or both eyes.

Causes of mono-ocular (one eye) blindness:

- Trauma to the eye.
- Central retinal artery occlusion.
- Central retinal vein occlusion.
- Giant cell arteritis.
- Optic neuritis or retrobulbar neuritis.
- Acute ischaemic optic neuropathy.
- Migraine.
- Others include acute glaucoma, retinal detachment and Leber OA, functional.

Causes of binocular (both eyes) blindness:

- Bilateral occipital lobe infarction.
- Bilateral occipital lobe trauma.
- Bilateral occipital nerve damage.
- Methyl alcohol poisoning, may be in quinine and ethambutol toxicity.
- Functional (hysteria).

Q: What are the causes of gradual blindness?

A: As follows:

Causes of bilateral blindness of gradual onset

- Cataract.
- Macular degeneration.
- Diabetic retinopathy (vitreous haemorrhage).
- OA.
- Bilateral optic nerve or chiasmal compression.
- Bilateral optic nerve damage (tobacco amblyopia).

Methanol Poisoning

Methanol is a component of varnishes, paint remover, wind shield washer solutions and copy machine fluid. Methanol is metabolized by alcohol dehydrogenase to formaldehyde and formic acid. It is mainly metabolized in liver (90%), only 10% is excreted unchanged by lungs and kidneys.

Clinical features of methanol poisoning are:

- Early manifestations (by methanol): Nausea, vomiting, abdominal pain, headache, vertigo, dizziness, convulsion, confusion, stupor and coma.
- Later on (by metabolite formic acid): Retinal injury leading to blindness. There is metabolic acidosis. Ocular toxicity occurs 15–19 hours after ingestion.
- In severe cases: Bradycardia, myocardial depression and shock.

Treatment:

- Gastric lavage.
- Supportive measures: IV fluid, oxygen.
- Correction of acidosis: Sodibicarb in large dose (alkalinization enhances formic acid excretion).
- In early stage: Ethanol is given (it inhibits methanol oxidation by competing the inhibition of enzyme). Ethanol is given 10 mL/kg of 10% ethanol IV or 1 mL/kg of 95% ethanol orally.
- Thiamine (100 mg QID), pyridoxine (50 mg QID) and folate (50 mg QID).
- Folinic acid 30 mg IV every 6 hourly. It reduces ocular toxicity (accelerates metabolism of formic acid).
- Dialysis: Indicated, if ingestion of methanol is >30 g or metabolic acidosis or blood methanol >500 mg/L.

CHAPTER 11

DERMATOLOGY

"This is a very testing part. It is more difficult than a written test"

– Talley & O'Connor

Introduction

In any clinical examination of medicine, a few common cases related to dermatology are frequently selected. Most of the diagnosis is obvious on visual impression. The concept of **inspection** is always a valuable starting point during examination of a patient in dermatological diseases.

With the patient's permission, undress the patient and remove the make-up, if possible. A magnifying lens is helpful. Good light, preferably natural, is more appropriate. Feeling the skin provides diagnostic clue.

Examine the patient very carefully and gently. Describe the lesion precisely as follows: distribution, colour, size and shape, oozing, pattern of lesion (linear, ring-like, reticulated, annular and so on). After inspection, palpate to see tenderness, consistency, temperature and mobility.

Usual instructions are:

- "Perform the general examination of this patient" or "look at here" (examiner may indicate a part).
- What is your diagnosis?
- What else do you want to examine?

In this chapter, a few common dermatological diseases are included with related questions and answers and a brief discussion. Candidates are advised to go through a lot of dermatological cases to develop their skill for spot diagnosis.

Skin consists of three layers:

1. Epidermis: It has 5 layers; from top to bottom, the layers are:
 - Stratum corneum (horny layer).
 - Stratum lucidum.
 - Stratum granulosum (granular layer).
 - Stratum spinosum (prickle cell or Malpighian layer).
 - Stratum basale (basal layer).
2. Dermis.
3. Hypodermis or subcutis.

Epidermis is an avascular stratified squamous epithelium, attached to dermis by basement membrane. Basal cells move outwards towards superficial horny layer, and the time taken is four weeks; 95% cells of epidermis are keratinocytes; the remaining 5% are Langerhans cells and melanocytes. There are a few Merkel cells. Dermis contains blood and lymphatic vessels, nerves, muscle, appendages (sweat glands, apocrine gland, sebaceous glands and hair follicles) and immune cells such as mast cells and lymphocytes. It also contains collagen, elastin and ground substance.

Functions of the skin:

1. Protection against chemicals, ultraviolet radiation (UVR), antigens and microbes.
2. Physical barrier against friction and shearing forces.
3. Preservation of a balanced internal environment (by preventing loss of water, electrolytes and macro-molecules).
4. Sensation (pain, touch and temperature).
5. Synthesis of vitamin D and testosterone.
6. Temperature regulation.
7. Body odour and psychosocial factors.

Psoriasis

Usual instructions are:

- Look at here, what is your diagnosis?

Presentation of a Case

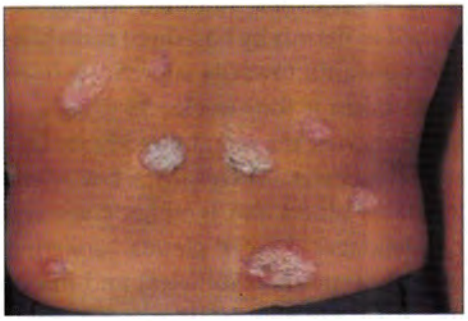
- There are multiple, well-circumscribed, erythematous plaques with silvery white scales at the knee, scalp and natal cleft (mention the site).

My diagnosis is **psoriasis.**

Q: What **else** do you want to examine?

A: I want to see:

- Nails: Pitting, oil spot, cracking of free edges, onycholysis (separation of nail plate from its bed), and thickening and subungual hyperkeratosis.
- Joints: Arthropathy (see page 408).
- Eye: Iritis (may be blepharitis, keratitis and conjunctivitis).
- Tongue: Geographical tongue.



Plaque psoriasis

Q: What are the **sites** of psoriatic skin lesion?

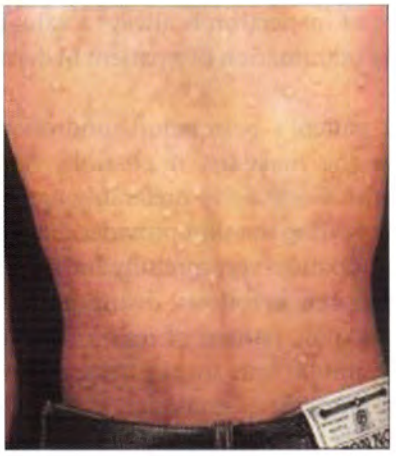
A: Extensor surfaces of knee, elbow, wrist, back of ear, scalp, hairline, extensor of limbs, sacrum, around the umbilicus, intergluteal cleft and flexures (natal cleft, axillary fold), submammary fold and nails.



Scalp psoriasis



Guttate psoriasis (front)



Guttate psoriasis (back)

Q: What are the **differential diagnoses** of psoriasis?

A: Psoriasis may be confused with the following diseases:

- Dermatomyositis (heliotrope sign, atrophy and poikiloderma).
- Lichen planus (usually on flexor surface, Wickham striae, violaceous flat-topped papules and adherent scale).
- Seborrhoeic dermatitis (greasy, yellowish scale on eye brows, nasolabial crease, gluteal crease, ears, sternal region, axilla, submammary folds, umbilicus and groin).
- Pityriasis rosea (short duration, herald patch and collarette scaling on trunk, upper arms and thighs).
- Subacute lupus erythematosus.

- Secondary syphilis.
- Dermatophytosis (tinea corporis, cruris and pedis).

Q: What is **Auspitz sign** and **Koebner phenomenon** in psoriasis?

A: As follows:

- Auspitz sign: On removing the scales forcibly, there are occurrences of capillary bleeding points.
- Koebner phenomenon: Psoriatic lesion is produced when the normal skin of a psoriatic patient is scratched or injured (may occur in surgical scar).



Koebner phenomenon



Auspitz sign

Q: What is Koebner **phenomenon**? What are the **causes** of Koebner phenomenon?

A: Koebner phenomenon is the appearance of isomorphic skin lesions at the site of trauma, burn or scratch mark. The causes are:

- Psoriasis.
- Lichen planus.
- Viral warts (verruca plana).
- Others: vitiligo, pityriasis rubra pilaris, molluscum contagiosum, nummular eczema and Darier disease.

Q: What are the **factors** that aggravate psoriasis?

A: The aggravating factors are:

1. Trauma.
2. Infections: β-haemolytic streptococci (aggravates guttate psoriasis) and HIV infection.
3. Psychological factors: emotion and anxiety.
4. Drugs:
 - β-Blocker.
 - Antimalarial (chloroquine and hydroxychloroquine).
 - Lithium.
 - Systemic steroid: the condition aggravates after withdrawal of steroid (rebound phenomenon) and also after stopping of the prolonged usage of local steroid.
 - Angiotensin-converting enzyme (ACE) inhibitor.
 - Alcohol.
5. Rarely, sunlight (UVR may worsen).
6. Metabolic (hypocalcaemia and dialysis).



Pustular psoriasis



Nail pitting

Read the Following Topics in Relation to Psoriasis

Q: What is **psoriasis**? What are the various **types** of psoriasis?

A: It is a chronic inflammatory disease of skin characterized by well-defined erythematous plaque with silvery white scales, involving commonly the extensor surface, elbows, knees and sacral regions associated with recurrence and remission. It affects 1–2% of the population.

There are four types:

- Chronic plaque psoriasis (Common. Well demarcated, red with a dry silvery white scale. It commonly involves elbow, knee and lower back, but may also involve scalp, nails, flexures, palms).
- Guttate psoriasis (raindrop like psoriasis is a variant, common in children and young adults. An explosive eruption of very small circular or oval plaques appears over the trunk about 2 weeks after a streptococcal sore throat. Majority of the patients develop plaque psoriasis in later life).
- Pustular psoriasis (It may be localized involving palm and sole or rarely generalized, which may be serious).
- Erythrodermic psoriasis (>90% of body surface area becomes red and scaly).

Q: What is the **pathology** of psoriasis?

A: Rapid proliferation and abnormal differentiation of epidermis (due to hyperproliferation of keratinocyte) and infiltration of inflammatory cells (polymorph, T-lymphocyte and other inflammatory cells). Accelerated epidermopoiesis is considered to be the fundamental pathological event in psoriasis.



Exfoliative dermatitis in psoriasis



Plaque psoriasis

Q: What **investigations** should be done in psoriasis?

A: As follows:

1. Routine:
 - Complete blood count (CBC).
 - Liver function test (LFT)
 - Serum creatinine.
 - Lipid profile.
 - X-ray chest.
 - Urine R/M/E (to see proteinuria).
 - Serum electrolytes (hypokalaemia, hyponatraemia, hypochloraemia).
 - Serum uric acid level.
 - Serum IgE (to differentiate from atopic dermatitis).
2. To establish the diagnosis, the following procedures may be performed:
 - Skin biopsy for histopathology (definitive).
 - Antistreptolysin O (ASO) titre (high in guttate psoriasis).
 - Throat swab culture and sensitivity (in guttate psoriasis).
 - X-ray of the affected joints (to examine psoriatic arthritis).
3. To exclude other causes, the following tests may be performed:
 - VDRL, TPHA, antinuclear antibody (ANA), anti SS-A, anti SS-B, direct immunofluorescence (DIF), uric acid and skin scraping for fungus.

Q: What are the **histological findings**?

A: As follows:

- Hyperkeratosis, parakeratosis, orthokeratosis.
- Neutrophilic micro-abscess of Munro in the stratum corneum.
- Granular layer is absent or thin over the dermal papilla.
- Spongiform pustule of Kogoj in stratum spinosum.

- Regular elongation of rete ridges, which are club shaped.
- Dermal capillary dilatation and tortuosity surrounded by a mixed neutrophilic and lymphohistiocytic perivascular infiltrate.

Q: What are the complications of psoriasis?

A: As follows:

- Psoriatic arthropathy.
- Exfoliative dermatitis.
- Secondary infection.
- Hyperuricaemia and gout.
- Others: amyloidosis, renal failure, hepatic failure and congestive cardiac failure (CCF).



Psoriasis vulgaris



Psoriasis in surgical scar



Psoriatic arthritis

Q: How to treat psoriasis?

A: As follows:

1. General measures:
 - Explanation and reassurance.
 - Avoid trauma, precipitating drugs and anxiety.
2. Specific treatment:
 - Local therapy.
 - Systemic therapy.
 - Combination therapy.

Local therapy (topical therapy on the lesion):

- Emollient: Common emollients are petrolatum, paraffin, urea (up to 10%), olive oil etc.
- Salicylic acid (≥5%): It is keratolytic, used to soften and remove scale from psoriatic plaques.
- Crude tar (3–5%): It inhibits DNA synthesis.
- Dithranol: It inhibits DNA synthesis.
- Calcipotriol: It is a vitamin D3 analogue. It inhibits epidermal proliferation and restores normal horny layer. It is very effective in the treatment of plaque type and scalp psoriasis. It may cause hypercalcaemia and hypercalciuria.
- Tazarotene: Third-generation topical retinoid. It acts by modulating keratinocyte differentiation and hyperproliferation, also by suppressing inflammation.
- Topical steroid (mildly potent to super potent according to severity of disease).
- UVR therapy: Narrow band UVB (peak emission around 311 nm) has been proved more effective than broadband UVB. However, it may cause burning.
- Tacrolimus and pimecrolimus: Helpful for thin lesions in areas prone to atrophy or steroid acne.
- Excimer laser: Indicated for patients with stable recalcitrant plaques particularly in the elbow and knee region.

Systemic therapy:

- PUVA (psoralen and UVA): Long-term use may cause squamous cell carcinoma, basal cell carcinoma and melanoma.
- Retinoid (acitretin): May help for arthritis and psoriasis (especially pustular and also plaque). Avoid in young female patients (it is teratogenic).
- Methotrexate, azathioprine or cyclosporine may also be used.

- Biologic agents: Commonly used drug is anti-TNF-α such as infliximab, etanercept, adalimumab and efulizumab.
- Other drugs: Tacrolimus, mycophenolate mofetil, hydroxyurea and thioguanine.

Combination therapy:

- MTX plus topical agent.
- MTX plus retinoid.
- Retinoid plus PUVA.
- MTX plus infliximab.

For nail disease:

- Systemic agents
- Topical retinoids
- Local triamcinolone injections
- Topical fluorouracil.

Q: Name the **drugs** that will help cure both psoriasis and arthritis.

A: Methotrexate, azathioprine and acitretin.

Erythema Multiforme and Stevens–Johnson Syndrome

Usual instructions are:

- Look at here, what is your diagnosis?

Presentation of a Case

- There are multiple erythematous, maculopapular, urticarial, vesicular and bullous lesions involving the skin of palm, leg and foot (mention the site), with few target lesions.

My diagnosis is **erythema multiforme**.

Q: What **else** do you want to examine? Why?

A: I want to see the oral cavity for mouth ulcer. If mouth ulcer is present associated with skin lesion, the diagnosis is **Stevens–Johnson syndrome (SJS)**.



Stevens–Johnson syndrome (face)



Stevens–Johnson syndrome (body)

Q: What is the **important** skin lesion in erythema multiforme?

A: Target lesion (also called **iris lesion** or **Bull's eye lesion**). In this lesion, there is central pallor or dusky purpura with oedema and peripheral redness.

Q: What are the **differential diagnoses**?

A: As follows:

- Drug reaction.
- Systemic lupus erythematosus (SLE).
- Pemphigus vulgaris or bullous pemphigoid.
- Dermatitis herpetiformis.
- Urticaria or urticarial vasculitis.

Q: What is **erythema multiforme**? What is **SJS**?

A: As follows:

- Erythema multiforme is an acute inflammatory reaction in the skin and mucous membrane, characterized by multiple erythematous skin lesions, such as macules, papules, vesicles, bullae

and target lesions involving the extensor surfaces of limbs. It is due to circulating immunocomplex that follows 7–14 days after precipitating factors (infections and drugs). It is usually self-limiting, resolves in 3–6 weeks, may recur.

- SJS is the severe form of erythema multiforme with widespread bullous lesion in skin and mucous membrane of mouth, eyes, and genitalia associated with severe constitutional symptoms.



Erythema multiforme (target lesion on hands)



Erythema multiforme (target lesion on buttock)

N.B. Remember the following points:

- SJS has <10% body surface area (BSA) involvement.
- 10–30% BSA involvement is called SJS-TEN (toxic epidermal necrolysis) overlap cases.
- When there is more than 30% of BSA involvement, it is called TEN. It is most commonly induced by the same medications. Patients who initially present with SJS may progress to TEN.

Q: What are the **causes of erythema multiforme**?

A: As follows:

- Infections: Herpes simplex virus type 1 (30% cases) and *Mycoplasma pneumoniae* (common). Other infections include *Streptococcus* and *Histoplasma*.
- Drugs: Sulfonamides, carbamazepine, thiacetazone, barbiturate, penicillin, phenytoin and phenylbutazone.
- Idiopathic (50% cases).
- Others: Malignancy (carcinoma and lymphoma), collagen disease (SLE and dermatomyositis), Wegener granulomatosis, and sensitivity to vaccination (polio and BCG).

Q: What **history** do you like to take?

A: As follows:

- History of drugs.
- Infections.
- Any malignancy.
- Collagen disease.

Q: What **investigations** should be done in erythema multiforme?

A: As follows:

- Full blood count (FBC).
- ASO titre.
- Antibody to herpes simplex type 1.
- Antimycoplasma antibody.
- Other investigations according to suspicion of causes.

Q: How to **treat**?

A: As follows:

- Offending drugs should be stopped.
- Symptomatic (IV fluid, antipyretic and antibiotic).
- Local care of eyes and mouth.
- Treatment of primary cause.
- In severe cases, especially in SJS, IV immunoglobulin can be given.
- Aciclovir (for recurrent herpes simplex infection).
- Steroid: Its use is controversial. However, it can be used and should be tapered rapidly because once skin loss occurs, it may aggravate morbidity and mortality of the disorder due to immunosuppression.

Q: What is **bullous** lesion? What are the **causes** of bullous lesion of the skin?

A: Bulla is a circumscribed, fluid-filled elevation of skin more than 1 cm in diameter. The **causes** are:

1. The commonest causes are:
 - Erythema multiforme.
 - Pemphigus vulgaris.

- Bullous pemphigoid.
- Dermatitis herpetiformis.

2. Others:
 - Bullous impetigo.
 - Insect bite.
 - Congenital, epidermolysis bullosa.
 - Porphyria cutanea tarda.
 - Staphylococcal scalded skin syndrome (SSSS) and toxic epidermal necrolysis.
 - Diabetic bullous lesions of skin.



Toxic epidermal necrolysis

Q: What is Nikolsky sign?

A: Rubbing of uninvolved skin results in the separation of epidermis of the skin and this condition is called Nikolsky sign. The causes are pemphigus vulgaris (the commonest cause), pemphigus foliaceus, TEN, SSSS and epidermolysis bullosa (dystrophic type).



Nikolsky sign in pemphigus

Dermatitis Herpetiformis

Presentation of a Case

- There are multiple grouped, symmetrical, erythematous, polymorphous, papular, papulovesicular, vesiculobullous or bullous, urticarial and excoriated skin lesion on the extensor surface of knee, elbow, buttock, scalp, upper back and sacrum.

My diagnosis is **dermatitis herpetiformis**.

Q: What is the commonest **symptom**?

A: Severe itching.

Q: What **history** do you like to take and why?

A: Diarrhoea or malabsorption after taking gluten-containing diet (oat, rye, wheat, barley). There may be coeliac disease, 10% of them may have dermatitis herpetiformis.

Q: What are the **differential diagnoses**?

A: As follows:

- Drug reaction (bullous).
- Erythema multiforme.
- SLE (bullous).
- Pemphigus vulgaris.
- Bullous pemphigoid.
- Others: scabies, contact dermatitis or atopic dermatitis.



Dermatitis herpetiformis (hand)



Dermatitis herpetiformis (back)

N.B. Remember the following points:

- Dermatitis herpetiformis is common in male, and the male to female ratio is 2:1.
- 80% of the patients have HLA B8/DRw3.
- Taking iodide and gluten-containing diet may precipitate an attack.
- Can occur at any stage of adult life, rare in childhood.
- Once occurred, it is recurrent.
- Oral mucosa: Involved rarely, mostly when bullae are numerous.
- Higher incidence of developing malignancy than in general population (small bowel lymphoma). Hypothyroidism may also occur.
- There may not be overt symptoms of malabsorption, though an abnormal D-xylose absorption may be found in 70% patients.
- Almost all patients have partial villous atrophy in jejunal biopsy, even if no gastrointestinal tract (GIT) symptoms are present.



Dermatitis herpetiformis (leg and foot)



Dermatitis herpetiformis (hands)

Q: What **investigations** should be done?

A: As follows:

1. Skin biopsy shows:
 - Infiltration of neutrophils, eosinophils, fibrin at dermal papilla and subepidermal vesicle.
 - Direct immunofluorescence in normal skin biopsy (perilesional) shows granular IgA deposition alone or with C_3 at the dermo–epidermal junction with accentuation in dermal papillae (IgM and IgG are occasionally observed).
2. Anti-endomysial and tissue transglutaminase antibody may be present in the serum. Antireticulin antibody may be present.
3. Endoscopic biopsy from duodenojejunal flexure to diagnose coeliac disease shows:
 - Short and wide villi (partial villous atrophy).
 - Total flat mucosa (subtotal villous atrophy).
 - Reduced height of epithelial cells and increased plasma cells in lamina propria and intraepithelial lymphocytes.
4. HLA-typing (HLA-B8 and HLA-DR3 are positive in 80% cases).
5. Therapeutic trial with dapsone may reduce itching.

Q: How to **treat** dermatitis herpetiformis?

A: As follows:

- Dapsone: 100–150 mg/day (start with 100 mg and increase the dose gradually to an effective level). May be required for life-long usage. Rapid relapse occurs once the drug is stopped. Dramatic clinical response occurs in 72 hours (a therapeutic test) and itching reduces quickly. Dose is decreased gradually. Maintenance dose prescribed is 50 mg/day.
- Gluten-free diet (avoid wheat, rye, oat and barley).
- Other drugs used: Sulphapyridine, sulphasalazine, colchicine, and tetracycline with nicotinamide.

Complications of dapsone therapy:

- Blood dyscrasia (haemolytic anaemia, agranulocytosis and methaemoglobinaemia).
- GIT upset.
- Hepatitis.
- Neuropathy.
- Skin rash or exfoliative dermatitis.

N.B. Dapsone should be avoided in glucose-6-phosphate dehydrogenase deficiency.

Q: What are the **associations** in dermatitis herpetiformis?

A: As follows:

- Coeliac disease.
- Malignancy (lymphoma).
- Thyroid disorder (hypothyroidism).

Herpes Zoster (Shingles)

Presentation of Case No. 1

- There are multiple vesicles or pustules, papules and few crusted lesions (in thoracic or lumbar region), which have not crossed the midline.

My diagnosis is **herpes zoster**.

Presentation of Case No. 2

- Same lesion along the distribution of the ophthalmic division of trigeminal nerve.
- There is redness and ulceration in the cornea (right or left eye).



Herpes zoster

My diagnosis is **herpes zoster ophthalmicus**.

Q: What is the **cause**?

A: It is due to reactivation of **varicella zoster virus** that lies dormant in dorsal root ganglion of sensory nerves, following chicken pox in childhood. Thoracic dermatome is commonly involved.

Q: What are the **sites** of lesion?

A: As follows:

- Dorsal root ganglia (when thoracic or lumbar dermatome is involved).
- Gasserian ganglia (trigeminal ganglia): in herpes zoster ophthalmicus.
- Geniculate ganglia (in Ramsay Hunt syndrome).



Herpes zoster (healed)

Q: What is the **percentage** of involvement of dermatome?

A: As follows:

- Thoracic: 55%.
- Cranial: 20% (trigeminal nerve commonly involved).
- Lumbar: 15%.
- Sacral: 5%.

Q: Why does **reactivation occur**?

A: As follows:

- Spontaneous.
- Immunocompromised state: Multiple myeloma, malignancy (lymphoma and leukaemia), HIV infection and steroid and cytotoxic drug therapy.

N.B. High-risk groups include the elderly and immunocompromised patients.



Herpes zoster (buttock)



Herpes zoster (thigh)

Q: What **history** do you like to take?

A: As follows:

- History of chicken pox in childhood.
- Immunocompromised disease (multiple myeloma, lymphoma and leukaemia).
- Diabetes mellitus.
- Drugs (steroid and cytotoxic drug).

Q: What are the **presentations** of herpes zoster?

A: As follows:

- Initially, burning discomfort or pain along the involvement of dermatome and dysaesthesia is present (when thoracic dermatome is involved on right side, it confuses with acute cholecystitis).
- After 3–4 days, redness followed by papule, vesicle or pustules occurs (lesions occur in cluster). Crust formation occurs after few days.

Q: What **investigations** are done to detect herpes zoster?

A: Diagnosis is usually clinical. Investigations are rarely necessary.

- Raising antibody titre.
- Viral culture (44% positive).
- Polymerase chain reaction (PCR; 97% positive).
- Tzanck smear from vesicle (75% positive).
- Histopathology shows intra-epidermal vesicle with large swollen cells called balloon cells.

Q: What are the **complications** of herpes zoster?

A: As follows:

- Post-herpetic neuralgia.
- Secondary infections: Meningoencephalitis, myelitis and motor radiculopathy (lumbar and brachial).
- Bowel and bladder dysfunction occurs, if sacral root is involved. Generalized herpes zoster (may occur in Hodgkin lymphoma, leukaemia, HIV and bronchial carcinoma).
- In ophthalmic herpes, corneal ulcer and iritis occur.
- Ramsay Hunt syndrome.
- Pleurisy, myocarditis and hepatitis.
- Others: Phrenic nerve palsy and muscle wasting. Rarely, purpura and necrosis of affected segments occur (purpura fulminans).

Q: How to **treat** herpes zoster?

A: As follows:

1. Local treatment:
 - Antiseptic powder (povidone-iodine), drying solution, calamine lotion and local aciclovir cream.
 - Topical idoxuridine: 5% solution during first 36 hours of eruption may help.
 - Local application of heat and gentle pressure may help.
2. Systemic:
 - Oral aciclovir (800 mg, five times daily for 1 week) or valacyclovir 1 g 8 hourly or famciclovir 500 mg TDS.
 - In immunocompromised patient: Intravenous (IV) aciclovir 10 mg/kg 8 hourly **plus** anti-varicella zoster immunoglobulin may be given.
 - In severe cases, prednisolone 30–60 mg/day may be given (it does not cause dissemination). Systemic steroid is contraindicated in immunocompromised host.
3. Interferon may help in limiting herpes zoster in patients with cancer.
4. A 4-week course with prednisolone may help to reduce post-herpetic neuralgia.



Herpes zoster ophthalmicus (right side)



Herpes zoster ophthalmicus (left side)

Q: How to **treat** post-herpetic neuralgia?

A: It occurs in 10% cases, common in the elderly.

- Gabapentin and amitriptyline (separately or in combination).
- Topical: 10% lidocaine gel or 5% lidocaine–prilocaine in patch may be given.
- If no response, transcutaneous nerve stimulation (TENS) may help.
- A 3-week course of systemic prednisolone 40–60 mg/day, taper in 3 weeks may be given, if there is no contraindication.
- If there is still no response and in severe cases, ablation of ganglia may be tried (permanent anaesthesia of that part may occur).

(Usually there is no response to analgesics. It may take long time to recover, even up to 2 years.)

Q: What is **Ramsay Hunt** syndrome?

A: It is the herpes zoster of geniculate ganglia characterized by:

- Rash in the external auditory meatus and palate.
- Ipsilateral VIIth cranial nerve palsy (lower motor neuron).
- Ipsilateral loss of taste and buccal ulceration.

Herpes Zoster Ophthalmicus

This commonly involves ophthalmic (first) division of trigeminal nerve and occurs in 20% cases. Pain, tingling and numbness around the eye followed by vesicular lesions are present.

The usual features are:

- Mucopurulent conjunctivitis.
- Episcleritis, scleritis or iritis.
- Keratitis, corneal ulcer or panophthalmitis.
- Pupillary distortion.
- Occasionally, optic atrophy and visual loss.
- Choroidoretinitis, secondary glaucoma and cicatricial lid scarring.

Treatment:

1. Local care of the eye:
 - Local 3% aciclovir ointment (five times daily) and idoxuridine 0.1% drop in eye.
 - Local antibiotic eyedrop.
 - Eye protection using sterile pad.
2. Oral aciclovir 800 mg, five times daily for 1 week.

(Consult with an ophthalmologist.)

Q: Which **cranial nerves** are involved in herpes zoster?

A: As follows:

- Trigeminal nerve (commonly ophthalmic division).
- Facial nerve.
- Vestibulo-cochlear nerve.

Acanthosis Nigricans

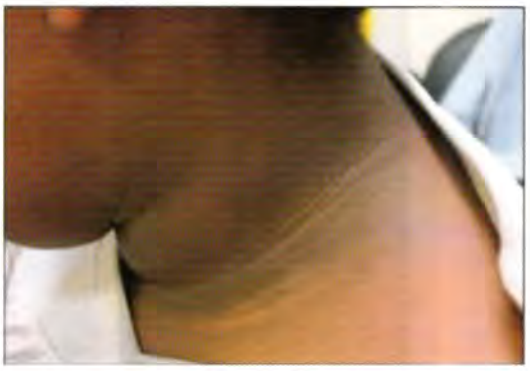
Presentation of a Case

- There are brown (or black), velvety plaques of skin (thick and rugose-like warts) in axilla, neck and limb flexures (may be found around the umbilicus, nipple and groins), which are symmetrically distributed.

My diagnosis is **acanthosis nigricans**.
(Rarely involves conjunctiva, buccal mucosa and lip when the lesion is extensive.)



Acanthosis nigricans (axilla)



Acanthosis nigricans (neck)

Q: What is **acanthosis nigricans**?

A: Acanthosis nigricans is a disorder of skin characterized by dark, thick, velvety skin in body folds and creases.

Q: What are the **causes** of acanthosis nigricans?

A: As follows:

1. In <40 years of age:
 - Obesity (commonest cause).
 - Insulin resistance.
 - Endocrinopathy (Cushing syndrome, acromegaly, hypo- and hyperthyroidism and polycystic ovary syndrome).
2. Above 40 years of age, it is commonly due to malignancy:
 - Carcinoma of stomach (the commonest cause) and other GIT malignancies.
 - Bronchial carcinoma.
 - Lymphoma.
 - In female: carcinoma of uterus, ovary, breast.

N.B. Remember the following:

- Acanthosis nigricans can affect otherwise healthy people. Sometimes, genetically inherited; it is common in people of African descent.
- Some drugs such as human growth hormone, oral contraceptive pills, steroid, fusidic acid can cause acanthosis nigricans.
- Besides, acanthosis nigricans may occur in various syndromes such as Bloom syndrome, ataxia–telangiectasia and Morfan (Mental retardation, pre- and post-natal overgrowth, remarkable face and acanthosis nigricans) syndrome.

Q: What is the relation between **acanthosis nigricans** and **malignancy**?

A: Acanthosis nigricans may occur before the development of malignancy in 18% or may parallel with malignancy in 60% and may follow malignancy in 22% cases. Remission occurs with cure of malignancy and worsens again with recurrence of tumour.

Q: What are the **types** of acanthosis nigricans?

A: As follows:

- Type I: acanthosis nigricans associated with malignancy.
- Type II: familial acanthosis nigricans.
- Type III: acanthosis nigricans associated with other diseases (e.g. obesity, insulin resistant state and endocrinopathy).

Q: How to **treat** acanthosis nigricans?

A: As follows:

- Treatment of primary cause.
- Reduction of weight, if obese.
- Topical application such as etretinate, tretinoin, calcipotriol, urea and salicylic acid.
- CO_2, laser ablation and long-pulse alexandrite laser therapy.

Q: What are the **dermatological manifestations** of malignancy?

A: As follows:

- Acanthosis nigricans.
- Dermatomyositis.
- Thrombophlebitis migrans (crops of tender nodules along the blood vessels): commonly associated with carcinoma of pancreas (body and tail).
- Ichthyosis.
- Tylosis (thickening of palm and sole and dysphagia).
- Exfoliative dermatitis.
- Erythema nodosum.
- Urticaria.

Ichthyosis

Presentation of a Case

- Skin of the affected area (mention the site) is rough, thick and dry.
- There are multiple fish-like scales.

My diagnosis is **ichthyosis**.

Q: What is **ichthyosis**?

A: Ichthyosis is the dry and rough skin with persistent visible scaling in the body, which may resemble fish scale.

Ichthyosis is not a single disease, but a group of diseases in which homeostatic mechanism of epidermal cell kinetics or differentiation is altered, resulting in the clinical appearance of scale.

Q: What does ichthyosis **indicate**?

A: It may be secondary to underlying malignancy or other diseases or due to the usage of some drugs.

Detailed history and physical examination should be done.

Q: What are the **types** of ichthyosis?

A: As follows:

1. **Congenital:**
 a. Major:
 - Autosomal dominant: Ichthyosis vulgaris and bullous ichthyosiform erythroderma.
 - Autosomal recessive: Lamellar ichthyosis and non-bullous congenital icthyosiform erythroderma.
 - X-linked ichthyosis.

 b. Minor: Harlequin foetus and ichthyosis linearis circumflexa.

 c. Syndromes: Refsum syndrome, Rud syndrome and Sjögren–Larsson syndrome.

2. **Acquired:**
 - Hodgkin and non-Hodgkin lymphoma, mycosis fungoides, multiple myeloma, leprosy, AIDS, dermatomyositis and SLE.
 - Drugs: Nicotinic acid, triparanol, butyrophenones and clofazimine.
 - Others: Sarcoidosis, hypothyroidism and nutritional deficiency.



Ichthyosis vulgaris (arm)



Ichthyosis vulgaris (back)



Ichthyosis vulgaris (face)



Ichthyosis vulgaris (legs)

Q: How to **treat** ichthyosis?

A: As follows:

- Treatment of primary cause.
- Symptomatic treatment with lactic acid, 12% ammonium lactate lotion, 10% urea cream, topical calcipotriene and so on.

Pemphigus Vulgaris

Usual instructions are:

- Look at here, what is your diagnosis?

Presentation of a Case

- There are multiple thin-walled blisters in the trunk, axilla and face.
- Some burst lesions, ulcer with crust and red margin are present.
- Mouth shows few ulcers.

My diagnosis is **pemphigus vulgaris**.

Q: What are your **differential diagnoses?**
A: As follows:

- Bullous pemphigoid.
- Stevens–Johnson syndrome.

Q: What is the **site** of lesion in pemphigus vulgaris?
A: In the epidermis (above the basal layer).

Q: What is **pemphigus vulgaris**?
A: It is an autoimmune blistering disease characterized by thin-walled, flaccid, easily ruptured bullae that appear in apparently normal skin and mucous membrane or on erythematous base (associated with mouth ulcer).

Q: What are the **causes** of pemphigus vulgaris?
A: Exact etiology is unknown. Probable factors are:

- Autoimmunity, as suggested by the intercellular deposition of IgG and C3 complement in epidermis.
- Genetic predisposition (associated with HLA DR4 and DR6).
- Drugs (penicillin, penicillamine, captopril, rifampicin, cephalosporin, pyrazolone etc).
- UV light, PUVA and ionising radiation.
- Increased incidence in myasthenia gravis and thymoma.

Q: What are the **types** of pemphigus?
A: As follows:

- Pemphigus vulgaris.
- Pemphigus foliaceus.
- Paraneoplastic pemphigus.
- IgA pemphigus.



Pemphigus vulgaris (thigh)



Pemphigus foliaceous (back)



Pemphigus foliaceous (face)

Q: What are the **presentations** of pemphigus vulgaris?
A: It is common in middle age, 50–60 years, and it is equally present in both sexes. Patients present with:

- Thin-walled flaccid bullae, which easily rupture, causing erosion, ulcer and crust formation with oozing and bleeding.
- Mouth ulcer is common (in 60%), also conjunctival and genital ulcer are noted.
- Ulcer heals slowly with hyperpigmented patch without scarring.

Q: What is the **bedside test** in pemphigus vulgaris?

A: As follows:

- Nikolsky sign: Rubbing of unaffected skin results in separation of epidermis.
- Bullae spread phenomenon or Asboe–Hansen sign: Pressure on the intact bullae gently forces the fluid to wander under the skin away from pressure site.

Q: What are the **investigations** done in pemphigus vulgaris?

A: As follows:

1. Routine:
 - FBC.
 - Blood sugar.
 - Urine RME.
 - Liver function tests.
 - Renal function tests.
2. Diagnostic:
 - **Skin biopsy** for histopathology and immunofluorescence test (an early intact bullae <12 hours duration should be taken with perilesional area).
 - Cytological (**Tzanck method**): Smears are taken from the base of a bulla and (using Giemsa stain) is used for rapid demonstration of acantholytic cell (which shows no intercellular bridge, darkly staining cytoplasm and large nuclei surrounded by lightly staining halo).
 - **Direct immunofluorescence** shows intercellular deposition of IgG throughout epidermis (both involved and normal skin) or oral mucosa and C3 deposition in acantholytic area (net-like, honeycomb or mosaic pattern).

Histological findings:

- Acantholysis (separation of individual keratinocyte from one another).
- Superficial intraepidermal split.
- Intraepidermal blister above basal layer (in pemphigus vulgaris) or subcorneal epidermal split (in pemphigus foliaceous).
- Acantholytic cells are found lining the bulla as well as lying free in the bulla cavity.
- Eosinophilic spongiosis and occasionally neutrophilic spongiosis may be seen in the spongiotic epidermis in pemphigus vulgaris.

Q: How **biopsy and DIF materials** are collected?

A: A small early intact bulla should be taken. Site of biopsy is frozen with aerosol refrigerant spray so that the punch may include firm tissue. Tissue for biopsy is taken in test tube containing formalin. Normal appearing perilesional skin is taken for DIF in saline soaked gauze.

Q: How would you **treat** the patient?

A: As follows:

1. General measures:
 - Bed rest.
 - Daily bath to remove thick crusts and foul odour.
 - Maintenance of fluid and electrolyte balance and nutrition.
 - Antibiotic and blood transfusion (if necessary).
2. Topical:
 - 1% silver sulfadiazine is applied topically.
 - Antiseptic mouth wash and viscous xylocaine are to be applied in the mouth.
 - Care of the eye.
3. Systemic:
 - High-dose prednisolone 100–200 mg/day. The dose should be tapered when remission occurs with no new blister. Maintenance dose is required for long time (may require life-long treatment). If new blister occurs during treatment, the dose of prednisolone should be increased.
 - Other treatment:
 - IV methylprednisolone 1 g/day for 5 days (pulse therapy).
 - Mycophenolate mofetil 1–1.5 g is given twice a day (commonly used as steroid sparing drug).
 - Other drugs: Azathioprine, cyclophosphamide, methotrexate, cyclosporine and dapsone.
 - In resistant case, IV immunoglobulin may be tried.
 - Biologic agents (infliximab, rituximab and etanercept).
 - Extracorporeal photochemotherapy.

Q: What is the **prognosis**?

A: Prognosis is bad, and recurrence is common with high mortality.

Q: What are the **complications** of pemphigus vulgaris?

A: Secondary bacterial infection (pneumonia, septicaemia), hypoproteinaemia, side effects of systemic prednisolone.

Bullous Pemphigoid

Usual instructions are:

- Look at here, what is your diagnosis?

Presentation of a Case

- There are multiple tense bullae in the trunk, axilla and limbs.
- Also some red and urticarial patches are present.
- Mouth with no ulcer.

My diagnosis is **bullous pemphigoid**.

Q: What is the **site of lesion** in pemphigoid?

A: The lesion is in the basement membrane between epidermis and dermis **(subepidermal)**, hence less tendency to rupture.



Bullous pemphigoid (body and arm)



Bullous pemphigoid (body)



Pemphigus vulgaris



Bullous pemphigoid

Q: What are your **differential diagnoses**?

A: As follows:

- Pemphigus vulgaris.
- Dermatitis herpetiformis.
- Stevens–Johnson syndrome.
- Toxic epidermal necrolysis (TEN).

Q: What **investigations** do you suggest?

A: As follows:

1. Routine:
 - Complete blood count.
 - Random blood sugar.
 - Urine R/M/E.
2. Confirmatory:
 - Tzanck test.
 - Skin biopsy for histopathology and DIF.

Q: How to **confirm** the diagnosis of bullous pemphigoid?

A: Skin biopsy for histopathology and direct immunofluorescence shows deposition of IgG and complement C3 at the basement membrane (in a linear pattern). Histopathological findings are:

- Subepidermal bullae.
- Absence of acantholysis.
- Superficial dermal infiltration of many eosinophils.

Q: What are the **presentations** of pemphigoid?

A: It is common in the elderly, >60 years. Patient presents with:

- Tense bullae, red urticarial patch, less rupture, with a tendency to heal, may be urticarial, mostly in trunk, limbs and flexures.
- Mouth involvement (rare, and in <20%).

N.B. Pemphigoid may be associated with lymphoma.

Q: How to **treat** bullous pemphigoid?

A: As follows:

1. General treatment: Bed rest, maintenance of electrolyte, adequate nutrition etc.
2. Steroid:
 - Prednisolone 0.5–0.75 mg/kg/day, should be tapered slowly over few weeks after clinical improvement (may be required to continue for 2–3 years).
 - Potent topical steroid can be given alone.
 - In severe cases, methylprednisolone 15 mg/kg IV daily for 3 doses.
3. Tetracycline 500 mg 6 hourly with nicotinamide 500 mg 8 hourly.
4. Other drugs include dapsone, azathioprine, methotrexate, cyclophosphamide, cyclosporine and mycophenolate mofetil.
5. IV immunoglobulin.
6. Antihistamine, if needed.

N.B. Bullous pemphigoid responds to lower dose of prednisolone.

Q: What are the **causes** of bullous lesion in skin with mouth ulcer?

A: As follows:

- Pemphigus vulgaris.
- Bullous pemphigoid.
- Stevens–Johnson syndrome.
- Toxic epidermal necrolysis.
- Behçet syndrome.
- Bullous SLE.

Q: How do you **differentiate** pemphigus vulgaris from bullous pemphigoid?

A: As follows:

Points	Pemphigus vulgaris	Bullous pemphigoid
Age	Middle age (50–60 years).	Elderly (>60 years), few in infants and children.
Distribution	Scalp, face, flexures, may be generalized.	Trunk, limb, flexures.
Mucosa of mouth conjunctiva and genitalia	Commonly involved (60%).	Rarely involved (20%), oral mucosa is involved usually.
Lesion	Intraepidermal flaccid bullae that rupture easily and has a less tendency to heal.	Subepidermal, large, tense blisters that do not rupture easily and has a more tendency to heal. Urticarial plaques, erythematous patches, papules and nodules may be found.
Asboe-Hansen & Nikolsky signs	Positive	Negative
Target antigen	Desmoglein 3, sometimes desmoglein 1	BP 230 and BP 180.
Antigens (kDa)	130 kDa and 160 kDa.	230 kDa and 180 kDa.
Direct immuno-fluorescence	Intercellular deposition of IgG and C3 in mosaic pattern (C3 only lesional).	Basement membrane deposition of IgG and C3 in linear pattern (C3 both lesional and non lesional).
Treatment	Steroid with higher dose.	Steroid with lower dose.
Prognosis	Variable prognosis. May be fatal due to treatment complications and sepsis. Recurrence is common.	Better prognosis. Does not affect general health. Usually self-limited over 5–6 year period, may be fatal in very elderly person.

Arsenicosis (Chronic Arsenic Toxicity)

Usual instructions are:

- Look at here, what is your diagnosis?

Presentation of Case No. 1

- There are multiple hyperpigmented areas (mention the site), with scattered hypopigmented area giving rise to **raindrop** appearance.

My diagnosis is **chronic arsenic toxicity (arsenicosis)**.

Presentation of Case No. 2

- As above. **Plus**
- Multiple hard papular and plaque-like lesions with hyperpigmentation involving ... (report the site),
- Hyperkeratosis of palm and sole (rough and thick).

My diagnosis is **chronic arsenic toxicity**.



Hyperkeratosis of palm



Hyperkeratosis of palm



Rain drop pigmentation



Hyperpigmentation with scaly lesions

Q: What are the **differential diagnoses**?

A: As follows:

1. For pigmentation:
 - Lepromatous leprosy.
 - Haemochromatosis.
 - Addison disease.
 - Xeroderma pigmentosum.
 - Guttate psoriasis.
 - Tinea versicolor.
 - Idiopathic guttate hypomelanosis.
 - Post-inflammatory hypopigmentation and hyperpigmentation.
 - Drug melanosis.
2. For keratosis:
 - Epidermodysplasia verruciformis.
 - Multiple corn or callosities.
 - Verruca vulgaris.
 - Hereditary palmoplantar keratoderma.
 - Acrokeratosis verruciformis.

Q: What is the **mechanism** of arsenic toxicity?

A: After absorption, arsenic is widely distributed to all the tissues of body; it combines with sulphydryl-containing substances and inhibits the activity of many enzymes. It interferes with cell enzymes, cell respiration and mitosis.

Q: What are the **clinical presentations** of arsenicosis?

A: As follows:

- Melanosis: Hyperpigmentation (generalized or localized) with few scattered hypopigmented areas giving rise to **raindrop** appearance.
- Hyperkeratosis of mainly palm and sole. May be multiple, punctate, hard, discrete, papule and verrucous plaque.
- Nails: Brittle, may show transverse white striae of finger nails **(Mee line)**.
- Hair: Dry, may fall off.
- Eye: Conjunctivitis.
- Nose: Rhinitis, epistaxis, nasal obstruction and septal perforation.
- It may involve any system of the body (liver, kidney, lung and heart).

Q: What are the **diagnostic signs** of arsenicosis?

A: As follows:

- Hyperkeratosis of palm and sole.
- Hyperpigmentation and hypopigmentation (on trunk and extremities) are the hallmarks.

Q: What are the **systemic effects** of chronic arsenic toxicity?

A: As follows:

1. GIT: Anorexia, nausea and vomiting.
2. Hepatic: Hepatomegaly, cirrhosis of liver and non-cirrhotic portal hypertension.
3. Central nervous system (CNS): Peripheral neuropathy, seizure, confusion and encephalopathy.
4. Haematological: Anaemia, leucopaenia and thrombocytopaenia.
5. Musculoskeletal: Myalgia, arthralgia and atrophy of extensor muscles causing wrist drop or foot drop.
6. Renal: Dysuria, anuria and renal tubular necrosis.
7. Heart: Cardiomyopathy, dysrhythmia and heart failure.
8. Vascular: Peripheral vascular insufficiency causing black foot disease.
9. Endocrine: Diabetes mellitus may be precipitated.
10. Malignancy:
 - Skin: Squamous cell carcinoma, basal cell carcinoma and Bowen disease.
 - Carcinoma of lung, kidney, urinary bladder, liver (angiosarcoma), prostate and colon.

Q: How to **confirm** chronic arsenic poisoning?

A: By measuring the arsenic concentration in hair, nail, urine and serum.



Palmar hyperkeratosis



Hyperkeratosis in sole

Normal value of arsenic:

- Blood: <3 mg/L (or 5–50 ppb/mg/L).
- Urine: 0.005–0.04 mg/L.
- Hair: 0.08–0.25 mg/kg (pubic hair is preferred due to lack of contamination).
- Nail: 0.43–1.08 mg/kg.
- Daily urinary excretion: <0.1 mg/L.

N.B. Remember the following points:

- Skin manifestation requires 1 year to develop.
- Systemic manifestations require 10 years to develop.
- Early signs of arsenic toxicity: Conjunctivitis, transient icterus and hyperhydrosis.

Q: What other **investigations** are done in chronic arsenic toxicity?

A: As follows:

- FBC.
- Urine for routine examination.
- Chest x-ray.
- Liver function tests.

- Renal function tests.
- ECG.
- EEG.
- Nerve conduction test.

Q: How to **treat** chronic arsenic toxicity?

A: As follows:

1. Drinking of arsenic contaminated water must be stopped.
2. High protein diet.
3. Antioxidant (vitamin A 50,000 IU, vitamin C 500 mg and vitamin E 200 mg daily for 3 months).
4. Vitamins and minerals supplement.
5. Vegetables and fresh fruits.
6. *Spirulina* (an alga colony), which is rich in high protein, may help to clear arsenic.
7. For skin lesion: Keratolytic emollients (salicylic acid, urea and retinoic acid), cryotherapy, electrocautery and laser therapy.
8. Drugs (chelating agent may be used):
 - D-penicillamine (250 mg TDS) for 3 months, or
 - Dimercaprol (BAL), dimercaptosuccinic acid (DMSA) and dimercaptopropane sulphonate (DMPS). BAL has a tendency to redistribute arsenic to brain and testes. DMSA and DMPS are more preferable because of their low toxicity.

 Dose:
 - DMSA 10 mg/kg/day for 7 days followed by 10 mg/kg/day three times for 14 days.
 - DMPS: 100 mg TDS to QDS for every alternate week for three courses.

Preventive therapy: Drinking water should be safe.

Scabies

Usual instructions are:

- Look at here, what is your diagnosis?

Presentation of a Case

- There are multiple erythematous, excoriated papules, vesicles, pustules and scratch marks involving the interdigital area, fingers, ulnar edge of the hand and anterior part of the wrist.

My diagnosis is **scabies.**

Q: What are the other **sites** of scabies?

A: Anticubital fossa, elbow joint, axilla, areola, around umbilicus, lower abdomen, genitalia, buttock and dorsum of foot (face and scalp are never involved except in infants, children and immunocompromised population).

Q: What is the **causative** organism?

A: *Sarcoptes scabiei.*



Scabies (in genitalia)



Scabies (hand)



Infected scabies



Scabies

Q: What are the **clinical presentations** of scabies?

A: As follows:

- Intense itching, mostly at night. This may be associated with secondary infection.
- Papular lesions, excoriations and burrows at the sites of predilection.
- Presence of the same disease among family members or associates.
- In women, itching of nipple associated with generalized pruritic papular eruption.
- In men, itchy papules in scrotum and penis.

The patient may present with typical classical features or atypical form or features of complication.

Q: What is the **diagnostic sign** of scabies?

A: Burrow, which is short, wavy, dirty appearing line, found in edge of fingers, toes or at the sides of hand and foot. Burrow contains female mites and eggs and faeces of the mite.

Q: How to **diagnose** scabies?

A: As follows:

- Usually clinical (hand lens is used to see burrow and mite).
- Microscopical examination by scraping from lesion to see the mites.

Q: What are the **differential diagnoses** of scabies?

A: As follows:

- Papular urticaria.
- Atopic dermatitis.
- Dermatitis herpetiformis.
- Pityriasis rosea.
- Pediculosis corporis.

Q: What are the **types** of scabies?

A: As follows:

1. Classical scabies.
2. Others:
 - Scabies in a clean person.
 - Scabies incognito.
 - Nodular scabies (pink, tan, brown or red nodules can be seen): Range from 2 to 20 mm in diameter. The mite is not present in the nodular lesion.
 - Crusted scabies (Norwegian): Atypical form, common in immunocompromised and institutionalized population. Lesion may be hyperkeratotic and crusted. Scaling is common, and pruritus may be less.
 - Bullous scabies.

Q: What are the **complications** of scabies?

A: As follows:

- Secondary bacterial infection.
- Eczematisation and lichenification.
- Post-streptococcal glomerulonephritis.
- Others: Urticaria, exfoliative dermatitis, acrophobia and vasculitis.

Q: How to **treat** scabies?

A: As follows:

1. Drugs:
 - Permethrin 5% cream: Single application (from neck to toe) may be repeated after 1 week.
 - 1% gamma benzene hexachloride lotion.
 - Benzyl benzoate 25% lotion (apply for consecutive 3 nights).
 - Monosulphiram 5–8% emulsion (apply for consecutive three nights).
 - 10% precipitated sulphur in white petrolatum (apply for consecutive three nights).
 - Crotamiton 10% lotion or cream.
 - Ivermectin may help in immunocompromised, crusted or Norwegian scabies (200 mg/kg in single dose).
 - Scabetic nodules may require intranodular corticosteroid injection.
 - Ivermectin orally can be used in cases where topical therapy is difficult or impractical (e.g. widespread infestations in nursing homes).
2. General measures:
 - Control of secondary infection.
 - For itching, antihistamine can be prescribed.
 - Scrub bath before the application of topical medicine.
 - Washing of the cloths and bed sheet.
 - Simultaneous treatment of the affected family members.

Q: What are the causes of **treatment failure** in scabies?

A: As follows:

- Improper dilution of topical medicine.
- Faulty method of application.
- Scrub bath not taken.
- Secondary bacterial infection is not controlled, if the clothes and bed sheets are not properly sanitized.
- If simultaneous treatment is not given to other affected members of the family.
- If personal hygiene is not properly maintained.

Lupus Vulgaris

Usual instructions are:

- Look at here, what is your diagnosis?

Presentation of a Case

- There is reddish-brown plaque (or nodules) with irregular margin in the right (or left) side of the face and surface is smooth and glistening with fine scaling over it.
- Non-tender, soft in consistency with atrophic scar in one place and spread in other.



Lupus vulgaris (papular form)

My diagnosis is **lupus vulgaris**.

Q: What are the **differential diagnoses**?

A: As follows:

- Sarcoidosis.
- Cutaneous leishmaniasis.
- Leprosy.
- Discoid lupus erythematosus (DLE).
- Dermatomyositis.
- Psoriasis.
- Rosacea.
- Deep mycosis.
- Wegener granulomatosis.
- Bowen disease.
- Lymphocytoma.

Q: What is **lupus vulgaris**?

A: It is a cutaneous tuberculosis (TB) occurring in a person with moderate or high degree of immunity, as a post-primary infection.

Q: What is the **common site**?

A: It commonly involves the skin of head and neck in 80% of the cases, particularly seen around the nose, also in arms and legs (in India, buttock and trunk are commonly involved). Looks like apple-jelly, when seen by a glass slide pressed against the lesion. Lesions heal with scarring and new lesions slowly spread out to form a chronic solitary erythematous plaque. Chronic lesions are at high risk of developing squamous cell carcinoma.



Lupus vulgaris (plaque form)



Lupus vulgaris (ulcerative)



Lupus vulgaris (ulcerative)

Q: What are the **clinical types** of lupus vulgaris?

A: The five types are:

- Plaque form.
- Ulcerative and mutilating form.
- Vegetating form.
- Tumour-like form.
- Papular and nodular form.

Q: What are the types of **cutaneous TB**?

A: According to the source of infection, there are four categories of cutaneous TB, and they are:

1. Inoculation TB (exogenous source): Primary inoculation complex, TB chancre, warty TB (verrucous cutis) and some lupus vulgaris.
2. Secondary TB (endogenous source):
 - Contiguous spread: Scrofuloderma
 - Auto-inoculation: TB orofacialis.
3. Haematogenous spread: Some lupus vulgaris, acute miliary TB, tuberculous ulcer and gumma or abscess.
4. Eruptive TB (tuberculids):
 - Micropapular: Lichen scrofulosorum.
 - Papular: Papular or papulonecrotic tuberculid.
 - Nodular: Erythema induratum (also called Bazin disease).

Q: What are the **atypical mycobacteria** causing cutaneous TB?

A: As follows:

- *Mycobacterium marinum* (responsible for swimming pool granuloma; it comes from swimming pool, lagoon or lake).
- Others are *M. scrofulaceum*, *M. gordonae*, *M. szulgai*, *M. avium*-intracellulare complex, *M. haemophilum*, *M. chelonea* and *M. ulcerans* (causes Buruli ulcer).

Q: What is the **relationship** of lupus vulgaris with TB in other organs?

A: As follows:

- 46% have tuberculous lymphadenitis.
- 15–20% have pulmonary TB and TB of bones and joints.

Q: What is the **pathogenesis** or **mode of infection** in lupus vulgaris?

A: As follows:

- It commonly occurs in normal skin, at the site of inoculation.
- Direct extension from underlying infected gland or joints.
- Lymphatic spread from mucous membrane of nose and throat.
- Haematogenous spread from other site.
- At the site of primary inoculation, also BCG vaccination or in the scar of scrofuloderma.

Organisms may remain latent in the skin for many years. Local trauma, nonspecific inflammatory change or immunocompromised disorder may be responsible for reactivation of cutaneous TB.

Q: How to **investigate**?

A: As follows:

- CBC and erythrocyte sedimentation rate (ESR).
- Mantoux test.
- Chest x-ray.
- Skin biopsy for histopathology.

Q: How to **treat**?

A: Standard anti-tubercular therapy should be given: four drugs for initial 2 months. In continuation phase: 4–10 months.

Lichen Planus

Usual instructions are:

- Look at here, what is your diagnosis?

Presentation of a Case

- This patient has flat-topped, pruritic and polygonal violaceous papules on the flexors of wrist, trunk, medial aspect of thighs and shins.
- Wickham striae and Koebner phenomenon are present (report, if any).
- Oral mucosa shows reticulated whitish (or violaceous) plaques consisting of pinhead papules on the inner aspect of cheeks.
- Nail shows longitudinal grooving, proximal and distal onycholysis, ridging and splitting.

My diagnosis is **lichen planus**.

Q: What are the **other causes** of flat-topped papules?

A: As follows:

- Lichen amyloidosis.
- Lichen nitidus.
- Lichen myxoedematosus.

Q: What is the **cause** of Wickham striae?

A: It is due to focal increase in the thickness of granular layer and total epidermis. It is better seen with a hand lens (and by aniline dye).

Different types of mucosal lesions:

- Ulcerative: 50%.
- Reticulate: 30%.
- Atrophic: 20%.

Q: What are the **causes** of lichen planus?

A: As follows:

- Idiopathic
- Drugs
- Hepatitis C infection predisposes to lichen planus.

Q: What are the **drugs** that may cause lichenoid drug reaction?

A: β-Blockers, thiazides, spironolactone, frusemide, ACE inhibitors, calcium channel blockers, antimalarials, heavy metals, arsenic, lithium, iodides.



Lichen planus (nails)



Lichen planus (leg and foot)

Q: What are the **types** of lichen planus?

A: As follows:

1. Morphological type:
 - Annular.
 - Linear.
 - Hypertrophic.
 - Atrophic.
 - Vesicobullous.
 - Ulcerative and erosive.
 - Actinic.
 - Follicular.
 - Lichen planus pigmentosus.
 - Guttate and perforating.
2. Special variants:
 - Lichenoid drug reaction.
 - Lichen planus pemphigoides.
 - Lichen planus and LE overlap.
 - Keratosis lichenoides chronica.
 - Lichen planus and malignant transformation.
 - Lichen planus and hepatitis C association.
 - Lichenoid reaction of graft versus host disease.

Q: What are the **differences** between lichen planus and lichen nitidus?

A: As follows:

Points	Lichen planus	Lichen nitidus
Size	Variable, usually large	1–2 mm
Shape	Polygonal	Round
Colour	Erythematous to violaceous	Shiny and discrete
Wickham striae	Present	Absent
Pruritus	Marked	Uncommon
Mucosal change	Frequently present	Rare

Q: How would you **differentiate** between lichenoid drug reaction and lichen planus?

A: As follows:

Points	Lichen drug reaction	Lichen planus
Site	Sun-exposed areas	Flexor areas
Lesions	Larger and scaly	Smaller
Wickham striae	Absent	Present
Alopecia	More	Less
Mucosal involvement	Less	More



Lichen planus (toes)



Lichen planus (mouth)

Q: What are the **differential diagnoses** of lichen planus?

A: Differential diagnoses of lichen planus depends on the type, and they are:

1. Hypertrophic:
 - Lichen simplex chronicus.
 - Psoriasis.
 - Lichen amyloidosis.
2. Annular:
 - Granuloma annulare.
 - Annular syphilis.
 - Annular psoriasis.
3. Linear:
 - Lichen striatus.
 - Linear morphea.
4. Atrophic:
 - Lichen sclerosus atrophicus.
 - DLE.
5. Guttate:
 - Guttate psoriasis.
 - Pityriasis rosea.
6. Oral:
 - Candidiasis.
 - Secondary syphilis.
7. Follicular:
 - Lichen spinulosus.
 - Lupus erythematosus.

Q: What **investigations** should be done in lichen planus?

A: As follows:

- Complete blood count.
- Viral marker for hepatitis B and C.
- Skin biopsy for histopathology and DIF.
- Liver function tests and renal function tests for therapeutic purpose.

Q: What are the **histopathological** and **DIF findings** in lichen planus?

A: As follows:

- Histopathology shows hyperkeratosis, beaded hypergranulosis and saw tooth pattern of epidermal hyperplasia. There is destruction of basal layer, which is squamatized. In superficial dermis, there is dense band-like infiltration of lymphocytes and melanophages. Civatte bodies represent necrotic keratinocytes.
- DIF shows clumps of IgM and less frequently IgA, IgG and C_3 subepidermally corresponding to Civatte bodies.

Q: How to **treat** lichen planus?

A: Treatment depends according to the type and extent of the disease, and they are:

1. General measures:
 - Avoid drugs like diuretics, β-blockers and antimalarials.
 - Protection from trauma.
2. Cutaneous lesions:
 - Topical steroid, and sometimes intralesional steroid.
 - Systemic therapy: In widespread lesions, systemic steroid 1 mg/kg/day for 7 days, then taper (40 mg for 7 days and 20 mg for 7 days).
 - Narrow-band UVB and PUVA.
 - Isotretinoin and acitretin (0.5–1 mg/kg/day).
 - Cyclosporine.
 - Mycophenolate mofetil.
3. Oral lesions:
 - Topical steroid in orabase, nystatin with clobetasol, topical tretinoin with steroid and 0.1% topical tacrolimus.
 - PUVA and 308 nm excimer laser.
 - Systemic: Hydroxychloroquine 200–400 mg/day for 6 months. Thalidomide 150 mg/day.

Other agents used in cutaneous lesions also improve oral lesions.

Q: What is the **course** or **prognosis** of lichen planus?

A: Two-thirds of the patients will have lichen planus of less than 1 year. Many patients get cured spontaneously within 1 year. Recurrence occurs in half of the patients.

Q: What are the **medical causes of itching**?

A: As follows:

1. Liver disease: Primary biliary cirrhosis, obstructive jaundice.
2. Chronic renal failure.
3. Haematological: Polycythaemia rubra vera (after warm bath), lymphoma (especially Hodgkin disease), leukaemia, multiple myeloma, iron deficiency anaemia.
4. Endrocrine cause: Hypothyroidism, thyrotoxicosis, diabetes mellitus (especially associated with candidiasis).
5. Any internal malignancy.
6. HIV.
7. Psychogenic.

Exfoliative Dermatitis

Usual instructions are:

- Look at here, what is your diagnosis?

Presentation of a Case

- The patient has generalized exfoliation and erythema involving different parts of the body (report the site). There is also oozing.
- Skin is dry and warm.
- Nails are brittle, yellowish with subungual hyperkeratosis, onycholysis and dystrophy.

My diagnosis is **exfoliative dermatitis**.

Q: What are the **clinical features** of exfoliative dermatitis?

A: As follows:

1. Cutaneous manifestations:
 - Extensive exfoliation, scaling covering more than 90% of the body surface, and pruritus with widespread erythema.
 - Skin thickening and loss of hair (often).
 - Nails may be dystrophic.
 - Palms and soles are involved, mucous membranes are usually spared, but mucous membrane of upper respiratory tract and conjunctiva may be involved.
2. Systemic manifestations:
 - Diarrhoea.
 - Anaemia, oedema and tachycardia.
 - Lymphadenopathy (due to reactive hyperplasia).
 - Hepatomegaly (in 7–37% cases).
 - Splenomegaly (in 3–23% cases).
 - Occasionally, gynaecomastia.



Exfoliative dermatitis in psoriasis



Erythroderma in psoriasis

Q: What are the **causes of erythroderma** in adults?

A: Primary or idiopathic and secondary to other disease.

The causes are:

1. Cutaneous disease:
 - Psoriasis.
 - Atopic dermatitis.
 - Neurodermatitis.

- Dermatophytosis.
- Contact dermatitis.
- Seborrhoeic dermatitis.
- Stasis dermatitis.
- Pityriasis rubra pilaris.
- Pemphigus foliaceus.

2. Systemic disease:
 - Lymphoma.
 - Leukaemia.
 - Carcinoma (of lung, rectum, other malignancy).
 - Multiple myeloma.
 - HIV infection.
 - Graft versus host disease.
3. Drugs: Barbiturate, carbamazepine, dapsone, sulphonamide, allopurinol, lithium, phenothiazines and thiazide.

Q: What are the **causes of erythroderma** in childhood?

A: As follows:

- Atopic dermatitis.
- Leiner disease.
- Bullous ichthyosiform erythroderma and non-bullous ichthyosiform erythroderma.
- Lamellar ichthyosis.
- Pityriasis rubra pilaris.
- Idiopathic.
- Drugs.
- Generalized dermatophytosis.
- Leukaemia.
- Childhood dermatomyositis.

Q: What is the **pathogenesis** of exfoliative dermatitis?

A: There is increased rate of epidermal turnover. The number of germinative cells and their absolute mitotic rate are increased. Transit time of the cells through epidermis is shortened. Consequently, more material is lost from the epidermis. Desquamated cells show increased amount of nucleic acids and their degenerative products, decreased amount of free amino acids and increased amount of soluble protein.



Exfoliative dermatitis (hand)



Exfoliative dermatitis (legs)

Complications of exfoliative dermatitis

1. Metabolic:
 - Loss of permeability barrier causes xerosis, water loss and dehydration. Marked scaling causes protein loss and hypoalbuminaemia.
 - Marked vasopermeability causes edema.
 - Marked vasodilatation causes chills, hypothermia and high output cardiac failure.
2. Other complications:
 - Secondary infection.
 - Electrolyte imbalance.
 - Dermatogenic enteropathy (diarrhoea).
 - Thrombophlebitis.

Q: What are the **causes of exfoliative dermatitis with nail changes?**

A: As follows:

- Psoriasis.
- Pityriasis rubra pilaris.
- Lichen planus.
- Dermatophytosis.
- Atopic dermatitis.

Q: What are the **investigations** done in erythroderma?

A: As follows:

1. CBC: Normochromic normocytic anaemia, leucocytosis, eosinophilia and ESR (high).
2. Urine (proteinuria).
3. Chest x-ray (to see pneumonia, lymphoma, sarcoidosis and carcinoma).
4. Total protein and albumin-to-globulin ratio (hypoproteinaemia, altered albumin-to-globulin ratio).
5. Serum IgE (high in some cases, e.g. atopic dermatitis).
6. Serum electrolytes (hypokalaemia and hyponatraemia).

7. Others (according to suspicion of causes):
 - Skin biopsy for histopathology and DIF.
 - Skin scraping for fungus and fungal culture (in dermatophytosis).
 - ECG and echocardiogram in suspected cases of heart failure.
 - Bone marrow examination (to exclude leukaemia and myeloma, secondary deposits).
 - USG of whole abdomen.
 - Test for HIV.
 - Computed tomography (CT) and magnetic resonance imaging (MRI), if needed.

Q: What are the **causes of hypoproteinaemia** in exfoliative dermatitis?

A: As follows:
- Increased protein loss via scaling or leaking through the skin.
- Protein losing enteropathy.
- Decreased synthesis and increased catabolism of protein.
- Dilution by increased plasma volume.

Q: How to **treat**?

A: As follows:
- General measures: Maintenance of fluid and electrolyte balance and nutrition and protein balance by high-protein diet. Intake and output monitoring, maintenance of environmental temperature and frequent bathing.
- Emollients and lubricants: Liquid paraffin, Vaseline and olive oil or 12% ammonium lactate.
- Symptomatic: Antibiotic to control infection, antihistamine to control pruritus and diuretics in case of oedema and cardiac failure.
- In severe persistent cases, systemic steroid may be given (triamcinolone acetonide 80 mg intramuscularly (IM) as initial dose, repeated on fourth, seventh and tenth day according to the condition of the patient).
- Other drugs: Methotrexate, cyclosporine and acitretin can be used in psoriatic erythroderma. Isotretinoin can be used in erythroderma caused by pityriasis rubra pilaris. Immunosuppressives such as azathioprine and cyclophosphamide may be required occasionally.
- PUVA therapy can be used in mycosis fungoides or psoriasis.
- Treatment of primary causes (lymphoma and leukaemia).

N.B. If possible, systemic steroid should be avoided due to the dangers of fluid retention, secondary infection, diabetes and other complications. They should be avoided in psoriatic erythroderma for they may provoke development of pustular psoriasis. Steroid should be used cautiously in atopic and seborrhoeic dermatitis.

Q: What is the **prognosis** of exfoliative dermatitis?

A: Depends on causes:
- Prognosis is good in drug-induced cases after the offending drug is withdrawn.
- Prognosis is poor in cases of idiopathic erythroderma.
- For patients with psoriasis, atopic dermatitis or seborrhoeic dermatitis, it may continue for months, respond slowly and tend to relapse.
- For the patients with underlying diseases or malignancy, prognosis depends on the outcome and the course of the disease process.
- The mean duration of the disease is 5 years with a median of 10 months.
- The overall mortality is 20–40%. In 20% of the fatalities, the cause of death is unrelated to erythroderma.

Alopecia

Usual instructions are:
- Examine the head. What are your findings? What is the diagnosis?

Presentation of Case No. 1

- There is discrete, well-circumscribed patch of hair loss over the scalp in different parts.
- Hair follicles are also seen.
- Eyebrows and eyelashes are present.

My diagnosis is **alopecia areata**.

Presentation of Case No. 2

- There is total loss of hair over the whole scalp.
- The eyebrows and lashes are also absent.

My diagnosis is **alopecia totalis**.

Q: What **else** would you like to examine?

A: Hair loss in other parts of the body.

Q: If there is **total loss of body hair**, what it is called?
A: Alopecia universalis.

Q: What is **alopecia areata**?
A: It is the localized loss of hair in the scalp. It may be due to autoimmune mechanism. Found in SLE, may be associated with other autoimmune diseases, such as Hashimoto thyroiditis, Graves disease, pernicious anaemia, diabetes mellitus and vitiligo.



Alopecia totalis



Alopecia areata

Q: What are the **types** of alopecia?
A: The three types are:
- Alopecia areata (localized loss of hair in the scalp).
- Alopecia totalis (hair loss of entire scalp).
- Alopecia universalis (total loss of body hair).

Q: What are the **diagnostic points** of alopecia areata?
A: The following points are diagnostic:
- Usually patches are 1–5 cm in diameter.
- Rapid and complete loss of hair, which is patchy in distribution and round or oval in shape.
- At the periphery of bald patches, there are loose hairs that may be broken off leaving short stumps. When they are pulled out, a tapered attenuated bulb is seen as a result of atrophy of that portion; hence called **exclamation point hair**.
- Skin is smooth and shiny without any signs of inflammation and scaling.
- Pruritus is absent.
- In 10% cases, especially in long-standing cases with extensive involvement, nails develop uniform pits that may form transverse or longitudinal lines.

Q: What are the **differential diagnoses** of alopecia areata?
A: As follows:
- Non-inflammatory tinea capitis (characterized by multiple scaly lesions and stumps of broken hair and minimal inflammation; scraping from the scalp reveals hyphae of dermatophyte in microscopical examination in 10% KOH solution).
- Trichotillomania (inflammation and scaling are absent; circumscribed lesions are very rare).
- Alopecia of secondary syphilis and lupus erythematosus (history, clinical features, serological test, scalp biopsy and immunofluorescence confirm the diagnosis).

Read the following topics carefully.

Q: What are the **causes** of alopecia?
A: As follows:
1. Non-scarring (may be diffuse hair loss and focal hair loss):
 a. Diffuse hair loss:
 - Abnormality of shedding; telogen effluvium and anagen effluvium.
 - Endocrine: Hypopituitarism, hypothyroidism, hyperthyroidism, hypoparathyroidism, androgenetic alopecia and pregnancy.
 - Drugs: Cytotoxic drugs, anticoagulants, thyroid antagonists, lithium, oral contraceptives and hypervitaminosis A.
 - Others: Severe prolonged illness, malnutrition, deficiency of protein, iron, zinc and biotin, surgery, acute febrile illness and radiation.
 b. Focal hair loss:
 - Trichotillomania, traction alopecia, alopecia areata, secondary syphilis and SLE.
2. Scarring alopecia:
 - Infective: Furuncle, carbuncle, folliculitis, lupus vulgaris, tertiary syphilis, kerion and favus.
 - Physical factors: Burn and radiation.
 - Chemicals: Acid and alkali.
 - Autoimmune: DLE, morphea and cicatricial pemphigoid.

- Neoplastic: Basal cell carcinoma and squamous cell carcinoma.
- Others: Lichen planus, sarcoidosis, lichen sclerosus, follicular mucinosis, pseudopelade, folliculitis decalvans and dissecting cellulitis of scalp.

Q: How to **investigate** a case of alopecia areata?

A: According to clinical findings:

- Skin scraping for fungus (to exclude tinea capitis).
- ANA, anti-double-stranded DNA (SLE).
- Serological test for syphilis.
- Others: According to suspicion of causes.

Q: How to **treat** alopecia areata?

A: As follows:

1. Topical:
 - Topical steroid.
 - 1% anthralin cream.
 - Topical minoxidil (2–5%).
2. Intralesional injection of steroid (triamcinolone 2–10 mg/mL).
3. Photochemotherapy using topical or systemic methoxsalen and UVA (PUVA).
4. 308 nm xenom chloride excimer laser has been reported to produce regrowth after 11–12 sessions over a period of 9–11 weeks.

Q: What is the **prognosis**?

A: Usually, spontaneous recovery occurs in postpubertal patients. Predictors of poor prognosis are:

- Presence of atopic dermatitis.
- Childhood onset.
- Widespread involvement.
- Duration longer than 5 years.
- Onychodystrophy.
- Ophiasis (loss may occur confluent along the temporal and occipital scalp).

Vitiligo

Usual instructions are:

- Look here. What are your findings? What is the diagnosis?

Presentation of a Case

- There are few areas of depigmentation of variable size and shape, surrounded by area of hyperpigmentation.

My diagnosis is **vitiligo**.

Q: What **else** do you want to see?

A: Check for vitiligo in other parts of the body (around the eyes, mouth, knee, dorsum of foot, hands, axilla, groin and genitalia). Also, check the sensation (if lost, suggest tuberculoid leprosy. In advance stage with widespread vitiligo, loss of sensation may occur in lepromatous leprosy).

Q: What is **vitiligo**? What is the **mechanism**?

A: It is the area of localized depigmentation, probably due to autoimmune mechanism. Vitiligo is due to focal loss of melanocyte. It affects 1% of the population. Generalized vitiligo may occur, usually symmetrical involving hand, wrist, knee, neck, around the eyes, mouth, dorsum of feet and so on. The sites at friction or trauma are often affected. Family history may be present in one-third cases; it equally affects both sexes. Although familial in 30% cases, it is not inherited as autosomal dominant, or recessive trait, rather seems to have multifactorial genetic basis. Individual is otherwise healthy. Koebner phenomenon may be present (lesions appear at the site of skin damage).

Q: What are the **associated diseases** in vitiligo?

A: Vitiligo may be associated with autoimmune diseases, such as systemic sclerosis, Addison disease, pernicious anaemia, Graves disease, Hashimoto thyroiditis, premature ovarian failure, diabetes mellitus and primary biliary cirrhosis.



Vitiligo in fingers



Vitiligo in legs

Q: What are the **types** of vitiligo?

A: As follows:

1. Focal vitiligo: Isolated macules or few scattered macules.
2. Segmental vitiligo: Unilateral macules in a dermatomal distribution. It has stable course and is unlikely to be associated with thyroid or other vitiligo-associated diseases.
3. Generalized vitiligo: Most common, characterized by few to many macules.
4. Acrofacial vitiligo: Involves distal digits and periorificial areas.
5. Universal vitiligo: Widespread vitiligo with few remaining normal pigmentation.

Q: What are the **differential diagnoses** of vitiligo (or, what are the causes of localized hypopigmentation)?

A: As follows:

- Tinea versicolor: Common in back and chest; it has a fine scale. Yeast and hyphal forms are present (detected with 10% KOH solution).
- Pityriasis alba: Associated with fine scale; lesion is poorly defined.
- Tuberculoid leprosy.
- Morphea and lichen sclerosis: Hypopigmented or depigmented area associated with a change in skin texture.
- Tuberous sclerosis (ash-leaf spot).
- Chemical leucoderma.
- Burn.

Q: What are the **investigations** done in vitiligo?

A: Diagnosis is clinical. Investigations are:

- Woods light examination shows chalky or ivory white fluorescence.
- Skin scraping for *Malassezia furfur* (to differentiate from tinea versicolor).
- Others: Blood sugar, thyroid function tests and serum cortisol can be done according to the suspicion of causes.

Q: How do you **treat** vitiligo?

A: As follows:

1. General measures:
 - Reassurance.
 - Use of sunscreen.
 - Use of self-tanning cream containing dihydroxyacetone.
2. Topical:
 - Steroid (betamethasone and clobetasol propionate).
 - Topical calcipotriene can be added to topical steroid.
 - 0.1% tacrolimus ointment in treating facial vitiligo.
3. Phototherapy:
 - Narrow band UVB.
 - Topical application of 8-methoxypsoralen followed by UVA.
4. Surgical:
 - Epidermal grafting or autologous minigraft.
 - Transplantation of cultured melanocytes can be applied in patients with segmental vitiligo or with stable vitiligo, which does not respond to other therapy.

N.B. Spontaneous re-pigmentation occurs in 15–25% cases.

Neurofibroma

Usual instructions are:

- Look at the patient. What is the diagnosis?
- Examine this patient.

Presentation of a Case

- There are multiple nodular lesions of variable sizes and shapes on the face, both forearms and hands.
- Also, multiple café-au-lait spots on the back of the trunk.

My diagnosis is **neurofibromatosis type I**.

Q: What **else** do you like to see?

A: As follows:

- Axillary freckling.
- Lisch nodule.



Neurofibroma

- Examination of the ear to exclude acoustic neuroma.
- Eyes for optic glioma.
- Spine for scoliosis.
- Blood pressure (may be associated with phaeochromocytoma).

Q: What is the **triad** of neurofibromatosis?

A: As follows:

- Neurofibroma.
- Café-au-lait spots.
- Lisch nodules.

Q: What is **neurofibroma**?

A: It is a benign tumour of peripheral nerves arising from neurilemmal sheath.

Q: What is **neurofibromatosis**?

A: It is an autosomal dominant disease characterized by multiple neurofibroma and skin lesions like café-au-lait spots and axillary freckling.

Q: What are the **types** of neurofibromatosis?

A: Two types:

- Type 1 or von Recklinghausen disease or peripheral.
- Type 2 or central.

Q: What are the **features of type 1** neurofibromatosis?

A: As follows:

- Multiple cutaneous neurofibroma.
- Café-au-lait patches (up to 5 may be found in normal person), 5 mm in prepubertal and 15 mm in postpubertal patients.
- Axillary freckling.
- Hamartoma of iris (Lisch nodules).
- Optic glioma.

Q: What are the **features of type 2** neurofibromatosis?

A: As follows:

- Bilateral acoustic neuroma.
- Glioma—cerebral or optic nerve.
- Meningioma.
- Spinal neurofibroma.
- Schwannoma.
- Juvenile posterior subcapsular lenticular opacity.

Q: What are **Café-au-lait spots**?

A: These are round to ovoid, pale yellow or brown macules, usually present on the trunk. May be 1 cm to more than 15 cm. Up to 5 may be present in a normal person.

Q: What is **Lisch nodule**?

A: It is a melanocytic hamartoma on the surface of iris, clear to yellow or brown. It increases with age, almost always present in patient older than 20 years.

Q: What is **plexiform neurofibroma**?

A: In this type, entire nerve trunk and its branches are involved in diffuse neurofibromatosis with overgrowth of overhanging tissues, leading to gross deformities in temporal and frontal scalp. Commonest site of plexiform neurofibroma are temporal region in relation to trigeminal nerve, upper eyelid and back of the neck.

Q: What are the **associated findings or complications** of neurofibroma?

A: As follows:

- Kyphoscoliosis.
- Lung cyst (honeycomb lung).
- Pseudoarthrosis and other orthopaedic abnormalities.
- Glioma, meningioma, medulloblastoma.
- Pheochromocytoma (in MEN Ia).
- Posterior mediastinal tumour called dumb bell tumour.
- Rarely, sarcomatous change (dangerous complication of neurofibromatosis).

Q: Is **biopsy** necessary for diagnosis?

A: No, diagnosis is done clinically.

Q: What is **phacomatosis**?

A: It is a group of diseases in which neurological abnormalities are associated with cutaneous disease. These are:

- Neurofibromatosis type 1.
- Tuberous sclerosis.
- Von Hippel–Lindau syndrome.
- Sturge–Weber syndrome.

Mycosis Fungoides

Usual instructions are:

- Look at the patient's back. Or, perform the general examination.

Presentation of a Case

- There are multiple, brownish red, indurated plaques of various size and shape over the upper back of the patient. The largest one is ... cm in diameter.
- Scratch marks are seen.
- Few nodular lesions are noted in the same area.

My diagnosis is **mycosis fungoides**.



Mycosis fungoides on back



Mycosis fungoides

Q: What else do you want to see?

A: I want to see lymph nodes (may be localized or generalized).

Q: What are your differential diagnoses?

A: As follows:

- Psoriasis.
- Eczematous dermatitis.
- Contact dermatitis.
- Drug eruption.
- Hansen disease (leprosy).
- Tinea corporis.

Q: What is **mycosis fungoides**?

A: This is a slowly progressive T cell lymphoma of the skin.

Q: How does it **present**?

A: Initially, it presents with non-specific scaly eruptions, which may be thick and plaque like, confused with eczema or psoriasis. May involve any area of the skin. Usually progress very slowly over many years from a plaque stage through to nodules and finally a systemic stage. Extracutaneous involvement (such as liver, lungs, spleen) and lymphadenopathy occur in advance stage only. It is more common in males, 5^{th} to 7^{th} decade.

Q: What are the stages of **mycosis fungoides**?

A: As follows:

- Stage I : Eczema or psoriasis like lesions.
- Stage II : Plaque like.
- Stage III : Nodules, ulcers, tumours.
- Stage IV : Lymphadenopathy with or without systemic involvement.

Q: What investigation should be done to **confirm** the diagnosis?

A: Skin biopsy (hallmark is malignant T cell or Sezary–Launter cells). There may be Pautrier micro abscess, atypical cells in epidermis, large hyperchromic cells with irregular nuclei called mycosis cell.

Q: What is **Sezary syndrome**?

A: It is a variant of mycosis fungoides associated with erythroderma. There are large mononuclear cells in the skin and blood. Its prognosis is poor. Extracorporeal photo therapy (with oral methoxsalen, lymphocyte enriched blood fraction to UVA light and reinfusion of the cells into the patients may be helpful).

Q: How to **treat** mycosis fungoides?

A: As follows:

1. Initially local therapy:
 - Corticosteroid, nitrogen mustard (mechlorethamine), bexarotene gel.
 - PUVA or narrow band UVB phototherapy.
2. After plaque stage: Electron beam radiation.

3. If the disease progresses: PUVA plus retinoid, PUVA plus interferon, bexarotene, α-interferon with or without retinoid, IL-12, denileukin or total skin electron beam may be used.
4. If all fails: Systemic anti-lymphoma chemotherapy may be required.

Q: What is the prognosis?

A: It progresses slowly, usually over decades. Prognosis is better in patient with patch or plaque stage disease and worse in patient with erythroderma, tumour and lymphadenopathy.

Tuberous Sclerosis

Usual instruction is:

- Look at the patient's back. Or, perform the general examination.

Presentation of a Case

- There are multiple pink or yellowish papules on the face involving cheeks, nasolabial fold, sides of the nose and chin. Also few nodules are present on the forehead.

My diagnosis is **tuberous sclerosis**.

Q: What are these **papules** on the face called?

A: These are angiofibroma called adenoma sebaceum.



Adenoma sebaceum in tuberous sclerosis



Shagreen patch of the same patient

Q: What **else** do you like to see?

A: As follows:

- Subungual fibroma (nodule arising from the nail bed).
- Shagreen patches (firm, flesh coloured, patches of leathery thick skin over the lower back).
- Ash leaf patches (hypopigmented areas of skin).
- Café-au-lait spots present in 30% cases.



Ash leaf patch in tuberous sclerosis

Q: What **history** do you like to take?

A: As follows:

- Family history of similar disease.
- History of convulsion and mental retardation.

Q: What is **tuberous sclerosis**?

A: It is an autosomal dominant disease characterized by classic triad of mental retardation (or learning disability), epilepsy and skin lesions.

Q: What other lesions may be **associated**?

A: As follows:

- CNS hamartomas: Cortical tubers and subependymal hamartomas. There may be cerebral glioma and calcification of basal ganglia.
- Retinal phacoma (glial mass).
- Hyperplastic gum.
- Benign rhabdomyoma of heart.
- Renal angiomyolipoma.
- Cysts in lung, liver, pancreas, kidneys and bones.

Q: What will you see in **skull x-ray**?

A: Tram-line calcification at the basal ganglia.

Q: How to treat?

A: No specific treatment. Symptomatic treatment for seizure. Genetic counseling should be done.

Q: What is the cause of death?

A: Usually from seizure, intercurrent illness or associated neoplasm.

Kaposi Sarcoma

Usual instruction is:

- Look at the patient's back. Or, perform the general examination.

Presentation of a Case

- There are multiple red or purple or brownish plaques and nodules of various sizes and shapes all over the back.

My differential diagnoses are:

- Haemangioma.
- Bacillary angiomatosis.
- Cutaneous mycobacterial infection.
- Drug rash.
- Sarcoidosis.
- Cutaneous lymphoma.
- Kaposi sarcoma.



Kaposi sarcoma



Kaposi sarcoma

Q: What is Kaposi sarcoma?

A: It is a tumour of vascular and lymphatic endothelium characterised by multiple purplish nodules and plaque caused by human herpes virus 8 (HHV8). It is an AIDS defining illness.

Q: What is the cause?

A: Human herpes virus 8 (HHV8), also known as Kaposi sarcoma-associated herpes virus (KSHV). (70–100% of Kaposi sarcoma have antibody to HHV8 compared with 1–5% in general population).

Q: What are the types?

A: There are four types:

- Classic or sporadic form: Affects middle aged men, common in Jews and Mediterranean region, indolent course, mainly affects lower limbs, confined to skin and is not fatal.
- African endemic KS: Occurs in children and younger men, more aggressive and ultimately fatal. There is violaceous skin plaque, may be associated with generalized lymphadenopathy in children.
- Transplantation associated KS (or KS in iatrogenically immunocompromised patients)—especially in patients getting immunosuppressive therapy. It often regresses when the therapy is stopped.
- AIDS-related KS: More aggressive, often rapidly progress to plaques and nodules affecting the upper trunk, face, and oral mucosa. Affects one-third patients with AIDS, more common in homosexuals. About one-third develop a second malignancy like lymphoma, leukaemia, myeloma etc. In AIDS patient, it may occur with high CD4 count and low viral load.

Q: What is the presentation?

A: As follows:

- In early case: Small, raised, nonpruritic, reddish purple nodule on the skin or a discoloration of the oral mucosa or a swollen lymph node. Commonly affects lower limbs, back, face, mouth and genitalia. The cutaneous lesions can be solitary, localized or disseminated.
- With progression, the skin lesions become larger and numerous. The lesions may be macular, patch, plaque, nodular and exophytic.

- There may be chronic leg oedema.
- Visceral disease occurs in 10% at presentation. Commonly involved sites are lymph nodes, oral cavity, GIT, lungs, heart, CNS etc.

Q: How to diagnose?

A: Diagnosis is made with biopsy of suspicious lesion. If needed, internal imaging may be done.

Q: How to treat?

A: Depends on the subtype, localized or associated with systemic disease:

- Localized mucocutaneous disease responds to cryotherapy, radiotherapy, surgical excision, intralesional vinblastine, topical immunotherapy (imiquimod), interferon-α.
- AIDS-related KS: Patient should first get HAART, which improves Kaposi sarcoma.
- More widespread disease, or disease affecting internal organs, is treated with systemic therapy with interferon-α, liposomal anthracyclines or paclitaxel. IV chemotherapy (e.g. combination of vincristine and bleomycin or newer liposomal preparation of doxorubicin) and immunotherapy may be given.
- In KS from immunosuppression: Immunosuppressive therapy should be reduced or discontinued.

Pityriasis Versicolor

Usual instruction is:

- Look at the patient's chest. Or, perform the general examination.

Presentation of a Case

- There are multiple small hypopigmented macules over the front of the chest, both sides of neck and upper part of the back.

My diagnosis is **pityriasis (tinea) versicolor**.



Pityriasis versicolor in neck

Q: What is pityriasis versicolor? What is the cause?

A: It is a benign superficial skin condition characterized by multiple small white or pink macules. It is caused by a fungus called *Malassezia furfur*. It is common in warm temperature. It is more severe in immunocompromised.

Q: What are the differential diagnoses?

A: As follows:

- Vitiligo.
- Other fungal infections like tinea corporis.

Q: What are the sites of lesion of pityriasis versicolor?

A: Trunk, upper arm, neck, groin.

Q: How to confirm?

A: Skin scrapping for fungus with KOH, which shows large blunt hyphae and thick-walled budding spore (spaghetti and meatballs).

Q: How to treat?

A: As follows:

1. Topical treatment:
 - Selenium sulfide lotion applied from the neck to waist daily and kept for 5–15 minutes and continued for 7 days. Repeated weekly for a month and then monthly for maintenance.
 - Ketoconazole shampoo (1% or 2%): Applied and left for 5 minutes, may be used weekly.
 - Imidazole cream, solution or lotion may be used.
2. Oral antifungal:
 - Ketoconazole 200 mg daily for 1 week or 400 mg in a single dose.
 - Fluconazole 300 mg 2 doses 14 days apart.
 - Itraconazole may be given.

N.B. Recurrence is quite common. Maintenance treatment may be necessary.

CHAPTER 12

MISCELLANEOUS

"Experience is never limited, and it is never complete"

– Henry James

Face in Different Diseases

Usual instructions are:

- Look at the face; or, examine the face. What is your diagnosis? What relevant do you like to see?

There is likely to be obvious diagnosis by looking at the face. Further examination depends on the suspicion of the underlying cause. Possible diagnoses are as follows:

- Myxoedematous face (page 260).
- Thyrotoxic face or Graves disease (page 261 and 264).
- Cushingoid face (page 284).
- Acromegalic face (page 280).
- Mongoloid face (Down syndrome; page 507).
- Haemolytic face (frontal and parietal bossing, and prominent malar bones, page 247).
- Puffy face (page 503).
- Leonine facies (lepromatous leprosy, page 29).
- Facial palsy (page 367).
- Parkinsonian face (page 361).
- Marfanoid face (page 109).
- Mitral face (page 76).
- Myopathic face (page 359).
- Nephrotic face.
- Achondroplasia (skull appears enlarged, page 296).
- Superior vena caval (SVC) obstruction (page 30 and 31).
- Sturge–Weber syndrome (page 511).
- Hepatic facies (muddy or pigmented discolouration, pinched face and sunken eyes).
- Hippocratic facies (in advance peritonitis): sunken eyes, collapsed temples, pinched nose with crust on lips and clammy forehead.
- Psychiatric disorders (depressed or anxious facies).
- Butterfly rash (page 504).
- Systemic sclerosis (page 382).
- Myasthenic face (page 367).
- Turner face (page 505).
- Virile (virilization in female).
- Tabetic face.
- Paget disease.
- Facial asymmetry (hemiplegia and hemiatrophy).
- Lupus pernio in sarcoidosis.



Lupus pernio in sarcoidosis

Q: What are the causes of **depressed nasal bridge?**

A: As follows:

- Trauma.
- Tuberculosis (TB) (lupus vulgaris).
- Leprosy.
- Sarcoidosis.
- Congenital syphilis (also tertiary).
- Wegener granulomatosis.
- Fungal infection (deep).
- Idiopathic midline granuloma.
- Cutaneous leishmaniasis.



Depressed nasal bridge in Wegener granulomatosis

Q: What are the causes of puffy face?

A: As follows:

- Nephrotic syndrome.
- Acute glomerulonephritis (AGN).
- Myxoedema.
- SVC obstruction.
- Acromegaly.
- Angioneurotic oedema.
- Cushingoid face.
- Chronic alcoholism.
- Severe congestive cardiac failure.
- Hereditary angio-oedema.



Puffy face in nephrotic syndrome

Q: What are the causes of malar flush?

A: As follows:

- Normal person.
- Mitral stenosis.
- Hypothyroidism.
- Polycythaemia.



Malar flush

Q: What are the causes of plethoric face?

A: As follows:

- Polycythaemia (due to any cause).
- Cushing syndrome.
- Alcoholism.
- SVC obstruction.



Plethoric face in polycythaemia



Plethoric face in Cushing syndrome

Q: What are the causes of chloasma or melasma?

A: As follows:

It is a discrete pigmentation in the face of females, due to imbalance between oestrogen and progesterone. Melanocyte-stimulating hormone (MSH) is normal. The causes are:

- Pregnancy and sunlight exposure.
- Drugs (oral contraceptive and phenytoin).
- Others: ovarian tumour (rare).



Chloasma/melasma

Brief Notes on Wegener Granulomatosis

It is a disorder of unknown aetiology characterized by necrotising granulomatous vasculitis of upper and lower respiratory tract with glomerulonephritis.





Wegener granulomatosis

Diagnosis is made by:

History:

- Nasal discharge, epistaxis, nasal obstruction, nasal crust, rhinitis and sinusitis. If untreated, destruction of nasal bone and cartilage causes depressed nose.
- Deafness (due to serous otitis media).
- Respiratory problems: cough, haemoptysis and breathlessness.
- Eye: proptosis, conjunctivitis, episcleritis and iritis.
- Features of glomerulonephritis or renal failure.

Investigations:

- Chest x-ray: single or multiple nodules (migrating lung lesion in 50% cases).
- Biopsy: from nasal lesions or nasal crusts and also from kidney.
- Serum anti-neutrophil cytoplasmic antibody (c-ANCA) for diagnosis and to check the relapse.

Q: How to treat?

A: As follows:

- Cyclophosphamide (2 mg/kg) **plus** prednisolone (1 mg/kg), OR
- Intravenous cyclophosphamide (15 mg/kg) **plus** IV methylprednisolone (10 mg/kg) every fortnight and then every month.
- Once remission occurs (takes 3 to 6 months), prednisolone is rapidly reduced, and cyclophosphamide is replaced by azathioprine.
- Oral cotrimoxazole (960 mg, three times weekly) is given to prevent pneumocystis pneumonia.
- To check relapse, periodic measurement of c-ANCA is performed.

Butterfly Rash

Usual instructions are:

- Look at the face; or, examine the face.

Pay careful attention to the following points:

- Rash distribution (check whether present in other parts of face) and character, scaly desquamation and redness or other colour follicular plugging.
- Any nodular lesion (in face or ear lobule).
- Heliotrope rash (eyelid), telangiectasia, tightening or thickening of skin and pinched up nose.
- Alopecia.
- Mouth ulcer.

Presentation of a Case

- There are multiple skin rashes on the face along the butterfly distribution, also involving the forehead and cheeks (mention, if any). Some are scaly and reddish with clear margin, more marked on the right (or left) side of face.
- There is presence of nodule or telangiectasia, vitiligo and hyper- and hypopigmentation.



Butterfly rash (SLE)



Butterfly rash (dermatomyositis)

Q: What are the **differential diagnoses** for butterfly rash?

A: As follows:

- Systemic lupus erythematosus (SLE) or discoid lupus erythematosus (DLE).
- Dermatomyositis.
- Mixed connective tissue disease (MCTD).
- Sarcoidosis.
- Drug rash.
- Acne rosacea (characterized by red patch with telangiectasia on the face with papules and pustules, which are absent in SLE).
- Lepromatous leprosy.
- Post–kala-azar dermal leishmaniasis (PKDL).

Q: What else do you want to examine?

A: As follows:

- Rash in other parts of the body, alopecia and mouth ulcer SLE.
- Proximal myopathy (dermatomyositis).
- Sensation over skin lesion (leprosy).
- History of PKDL.
- History of drugs.
- Check for any lymphadenopathy, hepatomegaly, splenomegaly and erythema nodosum (sarcoidosis).



Skin rash in leg and foot (SLE)



Mouth ulcer in SLE

Turner Syndrome

Usual instructions are:

- Look at the patient. What is your diagnosis?

Proceed and Present as Follows:

(Ask the patient her age. The patient is a female with obvious short stature for her age.)

- Short and webbed neck, low hairline and redundant skinfold on the back of neck.
- Face: small lower jaw (micrognathia), small and fish-like mouth, high-arched palate and low set and deformed ears.
- Chest: broad, wide apart nipples (shield-like chest).
- Hand: short fourth metacarpal (other metacarpals may be short), lymphoedema of hands (also feet) and hypoplastic nails.
- Elbow: increased carrying angles (cubitus valgus).

My diagnosis is **Turner syndrome**.



Webbing of neck



Low hairline



Shield-like chest

Q: Why does **webbing** of the neck occur?

A: It occurs due to the fan-like fold of skin extending from shoulder to the neck or an abnormal splaying, out of trapezius muscle.

Q: What are the **causes** of webbing of the neck?

A: As follows:

- Turner syndrome
- Noonan syndrome
- Watson syndrome
- Klippel–Fleil syndrome
- Diamond–Blackfan anaemia

Q: What is **Turner syndrome**? How does the patient present?

A: It is a sex chromosomal abnormality, characterized by absence of one of the X chromosomes (45, XO). It only affects females. All or part of one X chromosome is deleted, leading to failure of ovary development. Externally, patient appears female, but does not produce female sex hormones. Hence, the patient remains sexually immature.

The patient usually presents with short stature, skeletal abnormalities and amenorrhoea. Secondary sexual characters are underdeveloped. Intelligence is usually normal.

Q: What **investigations** do you suggest?

A: As follows:

- Karyotyping from buccal smear: 45 (XO) is classical, occasionally 46 (XX) mosaics.
- Ultrasonogram (USG; small uterus, fallopian tube and streak gonad).
- Hormone assay (low oestrogen, high luteinising hormone [LH] and follicle-stimulating hormone [FSH]).

Q: What is **mosaicism**?

A: The presence of two or more cell lines within the body, either a 46XX or 46XY karyotype.

Q: How to **treat** Turner syndrome?

A: As follows:

- Oestrogen therapy at puberty.
- Growth hormone may accelerate height, but it is not yet established whether there is any effect on final height.
- Gonadal tumour may occur rarely, especially in mosaic involving Y chromosome. Hence, it should be removed.

Q: What are the **associations** or **diseases** that occur in Turner syndrome?

A: As follows:

1. Heart:
 - Coarctation of aorta (10–20% cases). There may be atrial septal defect (ASD), ventricular septal defect (VSD) and aortic stenosis (AS).
 - Hypertension.
2. Kidney:
 - Horseshoe kidney.
 - Hydronephrosis.
3. Others (incidence is more):
 - Diabetes mellitus (DM).
 - Hashimoto thyroiditis (may be frank hypothyroidism in 20% cases).
 - Lymphoedema in infancy.
 - Red and green colour blindness.
 - Strabismus and ptosis.
 - Premature osteoporosis.
 - Pigmented nevi.
 - Mental retardation (rare).

Noonan Syndrome

It is also called male Turner. Noonan syndrome is characterized by:

- Short stature.
- Mental retardation (common).
- Downward slanting and wide-spaced eyes.
- Low set ear.
- Webbing of the neck.
- Low posterior hairline.
- Pulmonary stenosis.

It may affect both male and female equally. Female patients have Turner phenotype but with normal 46, XX. They have normal ovarian function and normal fertility. In male, there is 46XY.

Cardiac lesion is present more on right side pulmonary stenosis (PS). In Turner syndrome, left-sided cardiac lesion is present more.



Short fourth metacarpal

Down Syndrome

Usual instructions are:

- Examine the patient. What are your findings? What else do you want to examine?

Proceed and Present as Follows:

1. Face:
 - Appears flat.
 - Nasal bridge appears flat.
 - Low set, small ears.
 - Mouth appears small and tends to remain open with high-arched palate. Tongue appears protruding with large, horizontal fissure.
2. Eyes:
 - Epicanthic folds and slanting eyes.
 - Brush-field spots on iris (yellow speckles).
 - Conjunctivitis.
3. Neck: short and wide.
4. Hands: single palmar crease (simian) and short stubby finger. Hand looks small and round (short, broad hands) and has clinodactyly (short inward curving of little finger).
5. Others: short stature, muscle tone (hypotonia), joint hyperextensibility, heart disease (VSD is common, also ASD, patent ductus arteriosus [PDA], tetralogy of Fallot and mitral regurgitation [MR] due to endocardial cushion defect), straight pubic hair, gap between first and second toes, and low IQ (from mild to severe).

N.B. The child is fond of music.



Down syndrome



Horizontal fissure in tongue



Single palmar crease in Down syndrome



Lymphoedema hand in Down syndrome



Lymphoedema foot in Down syndrome and gap between first and second toe

Q: What history do you like to consider?

A: Maternal age during pregnancy (incidence is high with advancing maternal age).

Q: What are the complications of Down syndrome?

A: As follows:

- Mental retardation (mild to severe). There is learning disability or cognitive impairment.
- Haematological: In neonates, acute myeloid leukaemia and in older children, acute lymphoid leukaemia.
- GIT: Duodenal atresia, Hirschsprung disease, Meckel diverticulum, imperforate anus.
- Presenile dementia of Alzheimer type (in third to fourth decade).
- Endocrine: Autoimmune hypothyroidism, diabetes mellitus type I.
- Infertility almost in all males, female may be fertile.
- Lenticular opacity.

Q: What is Down syndrome?

A: It is a chromosomal abnormality: trisomy 21 (47, XX/XY, + 21).

Q: How prenatal screening is done?

A: As follows:

1. First trimester:
 - Ultrasonography to see nuchal translucency.
 - Serum human chorionic gonadotropin (βhCG).
 - Pregnancy-associated plasma protein A (PAPP-A).
2. 13–20 weeks:
 - Maternal serum for α-fetoprotein, hCG and unconjugated oestriol (uE_3).
 - Foetal USG.
 - Amniocentesis.

N.B. Mother with risk of Down syndrome: Chorionic villous sampling before 13 weeks of gestation or amniocentesis after 15 weeks of pregnancy may be done.

Bilateral Parotid Enlargement

Usual instructions are:

- Look at the face of the patient. What is your diagnosis?

Presentation of a Case

- There is bilateral swelling of parotid glands, which are firm and nontender.

My diagnosis is **bilateral parotid enlargement.**



Bilateral parotid enlargement



Bilateral parotid enlargement

Q: What are the causes of bilateral parotid enlargement?

A: As follows:

- Sarcoidosis.
- Alcoholic liver disease or chronic alcoholism.
- Bilateral mumps (usually it is painful).
- Sjögren syndrome.
- Malnutrition.
- DM.
- Lymphoma.

- Leukaemia.
- Mikulicz syndrome.

Q: What **else** do you want to examine in this patient?

A: As follows:

- Dryness of eye and mouth (Sjögren syndrome).
- Lymph node (sarcoidosis, lymphoma and leukaemia).
- Other evidences of sarcoidosis (erythema nodosum and lupus pernio).
- Other collagen diseases (in secondary Sjögren syndrome).

Q: What is **Mikulicz syndrome?**

A: It is the enlargement of salivary and lacrimal glands. The causes are:

- Sarcoidosis.
- Lymphoma.
- Leukaemia.
- Tuberculosis.
- Sjögren syndrome.

Secondary Sjögren syndrome is called **Mikulicz disease** (where no salivary or lacrimal gland enlargement is present).

Xanthelasma

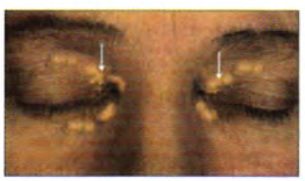
Usual instructions are:

- Examine the face. What does it present?

Presentation of a Case

- There are yellowish plaque or nodular lesions at the upper eyelid (may be also in lower eyelid), near the inner canthus in one or both eyes.

My diagnosis is **xanthelasma**.



Xanthelasma



Corneal arcus



Eruptive xanthoma



Tendon xanthoma (feet)



Tuberous xanthoma (elbow)



Tendon xanthoma (knuckle)



Tendon xanthoma in Achilles tendon



Tendon xanthoma (hands)



Tendon xanthoma in hands and leg

Q: What is **xanthelasma?** What are the **causes** of xanthelasma?

A: These are yellowish plaque in the subcutaneous or intracutaneous tissues due to deposition of cholesterol or lipids in the eyelids. The causes are:

1. Familial.
2. Primary biliary cirrhosis.
3. Hyperlipidaemia (types II and III).
4. Others
 - Hypothyroidism.
 - Diabetes mellitus.
 - Nephrotic syndrome.
 - Alcoholism.
 - Drugs (thiazide diuretic, cyclosporine, steroid, androgen and oral contraceptive pill).

Q: What **else** do you want to examine?

A: Corneal arcus, xanthoma in other parts (patella, Achilles tendon and dorsum of the hand) and evidence of primary disease.

Q: What is **xanthoma?** What are the various **types** of xanthoma?

A: Xanthomas are deposits of fatty material in the skin and subcutaneous tissue and tendons due to primary or secondary hyperlipidaemia. The four types are:

- Eruptive xanthoma (multiple, yellow or papule in trunk and buttock).
- Tendon xanthoma (subcutaneous nodules attached to tendons over dorsum of fingers and Achilles tendon).
- Tuberous xanthoma (elbow and knee).
- Palmar xanthoma.

Q: What are the **diseases associated** with hypercholesterolaemia and hypertriglyceridaemia?

A: As follows:

- Hypercholesterolaemia: Tendon xanthoma, tuberous xanthoma, xanthelasma, corneal arcus, atherosclerosis and ischaemic heart disease (IHD).
- Hypertriglyceridaemia: Acute pancreatitis, lipaemia retinalis and retinal vein thrombosis (alone it is not associated with atherosclerosis and IHD).
- Hypertriglyceridaemia associated with eruptive xanthoma.
- Mixed hyperlipidaemia: Tuberous, tendon, and palmar xanthoma.

Q: What are the **causes of lipaemia retinalis?**

A: Hypertriglyceridaemia and DM.



Lipaemia retinalis

Q: How to **treat** hypercholesterolaemia?

A: As follows:

1. General measures:
 - Weight reduction in obesity, exercise, diet (avoid cholesterol-containing diet and animal fat). Avoid smoking and alcohol. Treatment of primary disease.
2. Lipid lowering drugs may be given.
 Lipid-lowering drugs are:
 - HMG Co-A reductase inhibitors (simvastatin, pravastatin and lovastatin) are used in treating hypercholesterolaemia.
 - Fibrates (clofibrate, bezafibrate and gemfibrozil) are used in treating hypertriglyceridaemia.
 - Others: nicotinic acid, probucol and fish oil (omega-3 triglyceride).

N.B. Tendon xanthoma may be confused with:
- Rheumatoid nodule.
- Tophi of gout.
- Neurofibroma.
- Lipoma.

Sturge–Weber Syndrome

Usual instructions are:

- Examine the face. What are your findings? What is the diagnosis?

Presentation of a Case

- There is port-wine stain (reddish, slightly pigmented area) at the right outer part of face near the outer and upper part of right eye.

My diagnosis is **Sturge–Weber syndrome.**





Sturge–Weber syndrome

Q: What **history** do you like to take into consideration?
A: Epilepsy (on the side opposite to the skin lesion).

Q: What is **Sturge–Weber syndrome?**
A: It is a disease characterized by capillary or cavernous haemangioma (port-wine stain) along the cutaneous division of trigeminal nerve (commonly first or second division). There is venous haemangioma in subjacent leptomeninges, which may spread causing atrophy of cortex. It may be sporadic or inherited as autosomal dominant. Underlying brain damage is a rare cause of infantile hemiplegia, mental retardation and epilepsy. Lesion is on the face or the trunk in a dermatological distribution. In middle age, it may be dark with formation of angiomatous nodules. The patient may have mental retardation.

Q: What **investigations** do you suggest?
A: X-ray of the skull that shows **tramline** calcification (in cortical capillaries) and computed tomography (CT) or magnetic resonance imaging (MRI) investigations.

Q: What are the **findings in the eye** in Sturge–Weber syndrome?
A: As follows:
- Glaucoma (which may lead to blindness).
- Strabismus.
- Buphthalmos (ox-eye appearance).
- Optic atrophy.
- Angiomata of choroid.

Treatment: Unsatisfactory laser therapy for skin lesion.

Hereditary Haemorrhagic Telangiectasia

Usual instructions are:

- Examine the face. What are your findings? What is the diagnosis?

Presentation of a Case

- There is telangiectasia in lip, face, under surface of tongue, palate, buccal mucosa and nasal mucosa.

My diagnosis is **hereditary haemorrhagic telangiectasia** (also called Osler–Weber–Rendu syndrome).



Telangiectasia (tongue – on side)



Telangiectasia (tongue – undersurface)



Telangiectasia (toe and sole)



Telangiectasia (lip)

Q: What is **telangiectasia**? What are the **sites** of telangiectasia?

A: It is the localized collection of multiple non-contractile capillaries. If punctured, it shows prolonged bleeding time. It is found in lip, face, tongue (also under surface), buccal mucosa, nasal mucosa, nail bed, palm, feet, and gastrointestinal tract, also, in any part of the body (lungs, nervous system, liver etc).

Q: What are the **causes** of telangiectasia?

A: As follows:

- SLE.
- Dermatomyositis.
- Necrobiosis lipoidica diabeticorum.
- Systemic sclerosis.
- Carcinoid syndrome.
- Topical steroid.
- Ataxia telangiectasia.
- Hereditary haemorrhagic telangiectasia.

Q: What is **hereditary haemorrhagic telangiectasia**?

A: It is a disease inherited as autosomal dominant, characterized by the formation of multiple telangiectasia in the skin and mucous membrane in different parts of the body. It is a family disorder, caused by mutations in various genes. The disease is frequently heralded by recurrent epistaxis in early childhood. In some cases, telangiectasia in GIT may cause blood loss.

Sometimes, pulmonary arteriovenous (AV) fistula may develop resulting in haemoptysis, cyanosis and clubbing. Paradoxical embolism, stroke and cerebral abscess may occur. AV aneurysm may also occur in liver. In the eye, bloody tear (conjunctival telangiectasia), retinal haemorrhage, and even detachment may occur. Neurological telangiectasia may cause haemorrhage and the formation of bland or mycotic aneurysm.

Q: What are the presentations?

A: As follows:

- Epistaxis (common), usually recurrent and sometimes, the only site of bleeding.
- GIT bleeding.
- Haemoptysis.
- Bleeding from other sites.
- Anaemia (due to chronic blood loss, especially from GIT).

Q: How to treat HHT?

A: As follows:

1. General measures:
 - Continuous iron therapy.
 - Sometimes, blood transfusion in severe cases.
2. If epistaxis is the main symptom:
 - Oestrogen therapy (induces squamous metaplasia of nasal mucosa) is used.
 - Laser ablation.
 - Septal dermoplasty.
 - Antifibrinolytic agent (aminocaproic acid).
3. Skin lesion:
 - Cosmetic surgery
 - Laser ablation.
4. GIT: Photocoagulation therapy.
5. Lung arteriovenous malformation: embolization or ligation of the artery or surgical resection. (Individual lesions should not be cauterized.)

Yellow Nail Syndrome

Usual instructions are:

- Examine the fingers or toes. What are your findings? What is the diagnosis?
- Perform the general examination.

Presentation of a Case

- The nails are thick, curved from side to side and yellow (or greenish yellow) with onycholysis (separation of distal part of nail plate from its bed).
- Cuticles and lunulae are lost.
- Finger tips: bulbous and uncovered (stunted nail growth).

My diagnosis is **yellow nail syndrome**.



Yellow nail



Yellow nail syndrome (lymphoedema)

Q: What else do you like to examine?

A: Ankle oedema (non-pitting). Also, I want to examine the chest to check for bronchiectasis and pleural effusion (also may be chronic obstructive pulmonary disease [COPD] and malignant neoplasm).

Q: What is yellow nail syndrome?

A: It is an inherited disease associated with hypoplasia of the lymphatic system, characterized by thick and yellow nails and lymphoedema of legs.

N.B. Other associations of this syndrome are D-penicillamine therapy, nephrotic syndrome, hypothyroidism and acquired immunodeficiency syndrome (AIDS).

Normal Case

It is not uncommon that occasionally examiner may ask to examine a normal patient to assess the efficiency of a candidate's clinical skill or to see whether a candidate can examine systematically.

- It is frequently asked: "Examine the fundus of the patient". The candidate makes many **commissions** in a normal fundus.
- Examine the abdomen: There may not be any abnormality and you should present the case sincerely that there are no abnormal findings. However, remember that if the examiner asks to examine the abdomen again, probably some findings have been missed (just palpable liver, just palpable spleen and small abdominal mass). This time, examine very carefully.
- Examine the cardiovascular system (CVS): there may not be any abnormality in the heart, and the candidate make a "commission" of having murmur or rub.
- Perform the neurological examination; examine the reflexes, sensory test, cranial nerve and so on.
- Show how to see anaemia, jaundice, clubbing, oedema, lymph nodes, thyroid, pulse (quite common in under-graduate examination).

N.B. Remember the following points:

- Commission is dangerous than omission.
- Omission is safer than commission.

Section B

Common Interpretations in Medicine

CHAPTER 13

DATA INTERPRETATION

"A good clinician is a good physician. Clinical medicine will always persist as a basic diagnostic tool. Investigations, even sophisticated ones, will remain as complimentary to the clinician"

–The author

Hepatology

Case 01: Obstructive Jaundice

A 45-year-old male presented with the following blood report:

- Serum bilirubin: 20 mg/dL (normal up to 1.2 mg/dL).
- SGPT: 80 U/L (normal <20 U/L).
- Serum alkaline phosphatase: 1400 U/L (normal 20–100 U/L).
- Prothrombin time: 24s (control: 12s).

Q: What is the likely **diagnosis**?
A: Obstructive jaundice.

Q: Mention **three** important points in the **history** of the patient.
A: As follows:

- Generalized itching.
- Stool: Clay, pale or muddy coloured.
- Pain in the epigastrium or upper abdomen.

Q: Mention **one investigation** helpful for the diagnosis.
A: Ultrasonography (USG) of whole abdomen (or hepatobiliary system).

Q: Write down **four** important **causes** of this condition.
A: As follows:

- Choledocholithiasis.
- Carcinoma of the head of pancreas.
- Periampullary carcinoma.
- Cholangiocarcinoma.

N.B. High bilirubin with high alkaline phosphatase is highly suggestive of obstructive jaundice. Serum glutamic pyruvate transaminase (SGPT) may be slightly high. Other investigations like CT scan of abdomen, ERCP, MRCP may be necessary.

Case 02: Acute Viral Hepatitis

A 26-year-old man presents with anorexia, nausea and repeated vomiting for 3 days. He also noticed high-coloured urine and pain in right upper abdomen for 2 days. Investigation reveals:

- Hb 14 gm/dL, WBCs 3900/cmm, polymorphs 46%, lymphocytes 50%, eosinophil 4%.
- Serum bilirubin: 7.2 mg/dL (normal up to 1.2 mg/dL).
- SGPT: 800 IU/L (normal <20 IU/L).
- Serum alkaline phosphatase: 95 IU/L (normal 20–100 IU/L).

Q: Mention **two physical signs** you should look for.
A: As follows:

- Jaundice.
- Liver (enlarged and tender).

Q: What is the likely **diagnosis**?
A: Acute viral hepatitis.

Q: Mention **one investigation** that is helpful to see the prognosis.
A: Prothrombin time.

Q: Mention **two other investigations.**
A: As follows:

- Viral screening (HBsAg, anti-HAV, anti-HEV).
- Ultrasonogram of hepatobiliary system.

Q: Mention two other **differential diagnoses.**
A: As follows:

- Drug-induced hepatitis.
- Leptospirosis.

Q: Mention **two complications.**
A: As follows:

- Acute fulminating hepatic failure.
- Chronic liver disease.

Q: Mention **one serious complication.**
A: Acute fulminating hepatic failure.

N.B. With the above history and high bilirubin, high SGPT is suggestive of acute viral hepatitis. Alkaline phosphatase is normal or slightly high. Usually B and C infection may cause chronic liver disease. Hepatitis E may be serious, if associated with pregnancy.

Case 03: Haemolytic Jaundice

A 20-year-old man presented with high-coloured urine and yellow colouration of the whole body. There is no history of anorexia, nausea or vomiting. Laboratory investigations reveal:

- Hb 8 g/dL, WBCs 6600/cmm, polymorphs 65%, lymphocytes 20%, platelet count 1,80,000/cmm, ESR 95 mmHg in the 1st hour.
- Serum bilirubin: 3.2 mg/dL (normal up to 1.2 mg/dL).
- SGPT: 45 IU/L (normal <20 IU/L)
- Serum alkaline phosphatase: 250 IU/L (normal 20–100 IU/L)

Q: What is the likely **diagnosis?**
A: Haemolytic jaundice.

Q: Mention **three important physical findings** in this patient.
A: As follows:

- Anaemia.
- Jaundice.
- Splenomegaly.

Q: Mention **two haematological investigations** to find out the cause.
A: As follows:

- Peripheral blood film (shows microcytic hypochromic anaemia in hereditary haemolytic anaemia, macrocytic in autoimmune anaemia).
- Reticulocyte count (by supravital stain): High.

Q: Mention **two further investigations** to confirm your diagnosis.
A: As follows:

- Haemoglobin electrophoresis (to see type of hereditary haemolytic anaemia).
- Coombs test (to exclude autoimmune haemolytic anaemia).

N.B. Anaemia with high bilirubin but normal hepatic enzyme (normal SGPT, alkaline phosphatase) is highly suggestive of haemolytic anaemia. Mostly it may be due to hereditary haemolytic anaemia (e.g. thalassaemia major) or autoimmune haemolytic anaemia.

Case 04: Gilbert Syndrome

A young student presented with weakness, anorexia, nausea and high-coloured urine. He was suffering from sore throat 10 days back. There is history of previous similar attack. On examination: Anaemia – mild, jaundice – mild, liver – just palpable, nontender. Investigations show:

- CBC: Hb 10.2 g/dL, ESR 32 mm in 1st hour, WBCs 9900/cmm, polymorphs 61%, lymphocytes 35%, monocytes 4%.
- Reticulocyte count: 0.7% (normal 0.2–2%).
- Total bilirubin: 52 µmol/L (normal <17 µmol/L).
- Alanine transaminase (ALT) (SGPT): 15 IU/L (normal <20 IU/L).
- AST (SGOT): 21 IU/L (normal <25 IU/L).
- Alkaline phosphatase: 42 IU/L (normal 20–100 IU/L).
- USG of abdomen: Mild hepatomegaly.

Q: What is the likely **diagnosis?**
A: Gilbert syndrome.

Q: Suggest **two investigations.**
A: As follows:

- 48 h, 400 Kcal restriction test.
- IV 50 mg nicotine (there is rise of bilirubin).

Q: What **treatment** should be given in this patient?
A: As follows:

- Reassurance.
- Prolong fasting should be avoided.
- Therapeutic trial with phenobarbitone 60 mg TDS.

N.B. Recurrent jaundice but presence of normal liver enzymes in a young patient is highly suggestive of Gilbert syndrome. It is a type of unconjugated nonhaemolytic hyperbilirubinaemia, occurs in 2–7% of normal individual, some cases inherited as autosomal dominant. Most patients remain asymptomatic. Jaundice is usually mild and occurs intermittently during infection or prolonged fasting. Liver enzymes are normal and there are no signs of liver disease. It is due to defect in the uptake of bilirubin by the liver and also there is a deficiency of UDP-glucuronyl transferase activity, which conjugates bilirubin with glucuronic acid. Liver biopsy is normal. Other causes of nonhaemolytic hyperbilirubinaemia are Criggler–Najjar syndrome (type 1 and 2), Dubin–Johnson syndrome (liver is black due to increased deposition of lipofuscin and melanin) and Rotor syndrome.

Nephrology

Case 01: Acute Glomerulonephritis

A 12-year-old boy presents with scanty micturition and puffy face. Urine examination shows:

- Colour: Smoky.
- Albumin +.
- Pus cell 0–2/HPF.
- RBC 20–30/HPF.
- RBC cast: Present.

Q: What is the probable **diagnosis?**
A: Acute glomerulonephritis.

Q: Mention **one history** you should take.
A: History of sore throat 1–3-weeks back.

Q: Write down **three clinical signs** you should look for.
A: As follows:

- Periorbital oedema.
- Blood pressure (high).
- Lungs [bilateral basal crepitation: Indicates acute left ventricular failure (LVF)].

Q: Write **four further investigations.**
A: As follows:

- Blood urea and serum creatinine.
- Serum electrolytes.
- Ultrasonogram of renal system.
- X-ray chest (PA view).

Q: Mention **two complications.**
A: As follows:

- Acute LVF.
- Acute renal failure.

Q: Write down **principles of management.**
A: As follows:

- Salt and fluid restriction.
- Diuretic such as frusemide.
- Antibiotic: Penicillin.

N.B. History of sore throat followed by scanty, smoky urine associated with puffy face and periorbital oedema is highly suggestive of acute glomerulonephritis (usually poststreptococcal glomerulonephritis).

Case 02: Nephrotic Syndrome

A 7-year-old girl presented with swelling of the whole body with scanty micturition for 10 days. Her urine examination reveals:

- Colour: Straw.
- Albumin +++.
- RBC: Nil.
- Pus cell 0–2/high powered field (HPF).
- Fatty cast present.

Q: What is the likely **diagnosis?**
A: Nephrotic syndrome.

Q: Mention **three investigations.**
A: As follows:

- Serum total protein and albumin.
- 24 h urinary protein (>3 g).
- Serum lipid profile (there is high cholesterol and triglyceride).

Q: Mention **one drug** you think that should be given to this patient.
A: Prednisolone.

N.B. Generalized oedema, massive proteinuria and hypoalbuminaemia are suggestive of nephrotic syndrome. Commonest cause in children is minimal-change disease and in adult membranous or proliferative glomerulonephritis. Prognosis is better in children, but there may be relapse.

Case 03: Sterile Pyuria

A 40-year-old male presents with low-grade fever, weakness, loss of appetite and difficulty in micturition. Urine examination shows:

- Albumin +.
- RBC 5–6/HPF.
- Pus cell 50–60/HPF.
- Culture: No growth.

Q: What does the urine report **shows**?
A: Sterile pyuria.

Q: Mention **three causes**.
A: As follows:

- Renal tuberculosis.
- Partially treated urinary tract infection.
- Nongonococcal urethritis.
- Analgesic nephropathy.
- Tubulointerstitial nephritis.
- Prostatitis.
- Bilharziasis.

Q: Mention **two commonest causes**.
A: As follows:

- Renal tuberculosis.
- Partially treated urinary tract infection.

Q: Mention **four further investigations**.
A: As follows:

- Urine for acid fast bacteria (AFB) and mycobacterial culture.
- Ultrasonogram of renal system.
- Tuberculin test.
- Chest X-ray.

N.B. Presence of pus cells in the urine but sterile on culture is called sterile pyuria. Tuberculosis in the renal system is the likely cause.

Case 04: Acute Pyelonephritis

A 30-year-old female presents with high temperature, anorexia, nausea, vomiting, frequency of micturition and pain in the lumbar region. Urine examination shows:

- Albumin +.
- RBC few.
- Pus cell plenty.

Q: What is the likely **diagnosis**?
A: Acute pyelonephritis.

Q: Mention **one investigation** to confirm the diagnosis.
A: Urine culture and sensitivity.

N.B. Any patient with frequency, burning or difficulty in micturition associated with high temperature is suggestive of acute pyelonephritis. Treatment should be given according to culture and sensitivity of urine.

Case 05: Acute Interstitial Nephritis with ARF due to Cefixime

A 60-year-old male presented with fever, headache, dry cough, frequency of micturition and weakness for 10 days. Cefixime was given by a general practitioner. After 5 days, the patient complains of scanty urine, puffiness of face, swelling of legs, polyarthralgia and multiple skin rashes. Investigations reveal:

- Full blood count: Hb 10.9 g/dL, WBCs 11,200/cmm, polymorphs 64%, lymphocytes 28%, eosinophils 8%, ESR 110 mm in 1st hour, platelets 1,75,000/cmm.
- Urine: Pus cells – plenty, proteinuria (++); total protein 1 g/24 h.
- Urea: 19 mmol/L (normal 2.5–6.6 mmol/L).
- Creatinine: 833 µmol/L (normal 60–120 mmol/L).
- Serum electrolytes: Sodium 130 mmol/L, chloride 90 mmol/L, potassium 6.1 mmol/L, bicarbonate 17 mmol/L.

Q: What is your **diagnosis**?
A: Acute interstitial nephritis with acute renal failure (ARF) due to cefixime.

Q: Suggest two further investigations.
A: USG of kidney, renal biopsy.

Q: How to confirm the diagnosis?
A: Renal biopsy.

Q: How to manage this case?
A: As follows:

- Offending drug should be stopped.
- Prednisolone.
- Dialysis for ARF.

N.B. This patient presents with fever, skin rash, eosinophilia and renal impairment shortly after antibiotic therapy. These findings are consistent with acute interstitial nephritis. It is an acute inflammation of tubular interstitium, probably due to hypersensitivity reaction.

Neurology

Case 01: Tubercular Meningitis

A 25-year-old male presented with fever for 3 weeks and disorientation for 3 days. Cerebrospinal fluid (CSF) study shows:

- Pressure: High.
- Colour: Clear.
- Cytology: Total WBC 350/cmm, neutrophil 5%, lymphocyte 95%, no RBC.
- Biochemistry: Protein 300 mg/dL (normal up to 40 mg/dL), sugar 50 mg/dL (low).
- Microbiology: No organisms were found in Gram stains.

Q: What is likely diagnosis?
A: Tubercular meningitis.

Q: Mention four differential diagnoses.
A: As follows:

- Viral meningitis.
- Fungal meningitis.
- Sarcoidosis.
- Neurosyphilis or meningovascular syphilis.

Q: Mention one other investigation in CSF that is helpful for your diagnosis.
A: ADA (adenosine deaminase).

Q: What is the other finding in CSF?
A: If it is kept overnight, there is cob web appearance.

Q: Write down two important physical signs.
A: As follows:

- Neck rigidity.
- Kernig sign.

Q: What four other investigations will you suggest?
A: As follows:

- Complete blood count (CBC) with erythrocytic sedimentation rate (ESR).
- Tuberculin test.
- Chest X-ray (PA view).
- CT scan of head.

Q: What is the finding on fundoscopy?
A: Choroid tubercle in retina.

N.B. History of low-grade fever, weight loss and anorexia, along with signs of meningitis and typical findings in CSF (high lymphocytes, high protein and low sugar) is highly suggestive of tuberculous meningitis. It should be treated with standard antitubercular therapy for at least 9 months plus prednisolone 60 mg for 3 weeks and then should taper. Complications [e.g. cranial nerve palsy, hydrocephalus, syndrome of inappropriate antidiuretic hormone secretion (SIADH), seizure] may occur.

Case 02: Pyogenic Meningitis

A 19-year-old man presented with high-grade fever for 2 days and disorientation for 4 h. Neck rigidity and Kernig sign are present. CSF examination shows:

- Colour: Turbid.
- Pressure: Increased.
- Biochemistry: Protein 190 mg/dL, sugar 16 mg/dL, chloride 670 mg/dL.
- Cytology: Total cells 6200/cmm, polymorphs 96%, lymphocytes 4%.

Q: What is the likely **diagnosis**?
A: Pyogenic meningitis.

Q: What are the **causes** of bacterial meningitis?
A: As follows:

1. Neonate: Gram negative bacilli (*Escherichia coli*, Proteus), Group B streptococci, *Listeria monocytogenes*.
2. Preschool child: *Haemophilus influenzae, Neisseria meningitidis, Streptococcus pneumoniae, Mycobacterium tuberculosis*.
3. Older child and adult: *Neisseria* meningitidis, *S. pneumoniae, L. monocytogenes, M. tuberculosis, Staphylococcus aureus* (skull fracture), *H. influenzae*.

Q: What is the commonest **organism**?
A: *N. meningitides* (also called meningococcus).

Q: What are the **complications**?
A: As follows:

- Brain abscess.
- Hydrocephalus.
- Cranial nerve palsy.

Q: What other **physical findings** will you look in the body?
A: Skin rash such as petechial or purpuric, which indicates meningococcal septicaemia.

Q: If the patient develops **shock**, what is the likely cause?
A: Bilateral adrenal haemorrhage (Waterhouse–Friedriechson syndrome).

Q: What would you look for **before doing lumbar puncture**? Why?
A: I will do fundoscopy to see papilloedema (indicates raised intracranial pressure). If it is present, then lumbar puncture should be avoided because there may be herniation of cerebellar tonsils through foramen magnum, which compresses the vital centre in medulla oblongata and causes sudden death.

N.B. In any patient with high fever, headache, nausea, vomiting, photophobia with signs of meningism, it indicates pyogenic meningitis.

Case 03: Acute Viral Meningitis

A 24-year-old man presented with fever, headache, nausea, vomiting for 5 days. Neck rigidity and Kernig sign are present. CSF examination shows:

- Colour: Clear.
- Pressure: Increased.
- Biochemistry: Protein 60 mg/dL, sugar 50 mg/dL.
- Cytology: Total cell 100/cmm, polymorphs 2%, lymphocytes 98%.

Q: What is the likely **diagnosis**?
A: Acute viral meningitis.

Q: What are the common **organisms**?
A: Enteroviruses like Echovirus and coxsackie are the commonest.

N.B. Low-grade fever; headache; nausea; vomiting and CSF findings—clear, slightly high protein with normal glucose and chloride, with high lymphocyte is suggestive of viral encephalitis. There are usually no serious sequelae unless encephalitis is present.

Case 04: Subarachnoid Haemorrhage

A 45-year-old man presented with sudden, severe occipital headache followed by unconsciousness. Neck rigidity and Kernig sign are present. CSF shows:

- Colour: Red (frank blood).
- Pressure: Increased.
- Biochemistry: Protein 100 mg/dL, sugar 60 mg/dL.
- Cytology: Plenty of RBCs, polymorphs 60%, lymphocytes 40%.

Q: What is the likely **diagnosis**?
A: Subarachnoid haemorrhage.

Q: Mention two **causes**?
A: As follows:

- Rupture of berry aneurysm.
- Rupture of arteriovenous malformation.

Q: Mention one **fundoscopy** finding.
A: Subhyaloid haemorrhage.

Q: Suggest one **investigation**.
A: CT scan of head.

Q: Mention **two other investigations**.
A: As follows:

- Magnetic resonance angiography (MRA).
- Digital substraction angiogram (DSA).
- Cerebral angiography.

Q: Mention two **causes** of haemorrhagic CSF.
A: As follows:

- Subarachnoid haemorrhage.
- Trauma.
- Bleeding disorders like haemophilia, Christmas disease.

N.B. Sudden, severe thunderclap headache followed by unconsciousness is highly suggestive of subarachnoid haemorrhage. Control of hypertension, administration of nimodipine and surgical obliteration of the aneurysm by clipping is the mainstay of the treatment.

Haematology

Case 01: Acute Leukaemia

A 35-year-old lady presented with following blood report:

1. Hb 6 g/dL, ESR 70 mm in 1st hour.
2. WBC: 50×10^9/cmm.
 - Neutrophil: 35%.
 - Lymphocyte: 28%.
 - Monocyte: 03%.
 - Eosinophil: 05%.
 - Atypical cell: 29%.
3. Platelet: 100×10^9/cmm.

Q: What are the **abnormalities** in this blood picture?
A: Anaemia, leucocytosis with atypical cell, thrombocytopaenia, high ESR.

Q: What is the likely **diagnosis**?
A: Acute leukaemia.

Q: Mention one further **investigation**.
A: Bone marrow study.

N.B. Presence of atypical cell with high WBC count is suggestive of acute leukaemia, which may be either myeloid or lymphoblastic. Blast cell may be present.

Case 02: Chronic Myeloid Leukaemia

A 45-year-old man presented with weakness, loss of appetite and heaviness in the abdomen for 3 months. Laboratory investigation reveals:

1. Hb 9 g/dL, WBCs 1,50,000/cmm, polymorphs 45%, lymphocytes 8%, myelocytes 22%, metamyelocytes 14%, myeloblasts 3%, basophils 8%, platelets 2,10,000/cmm, ESR 90 mm in 1st hour.
2. PBF: Normocytic normochromic anaemia.

Q: What are the **abnormalities** in this blood picture?
A: Anaemia, leucocytosis with myelocyte and metamyelocyte, few blasts, high basophil and high ESR.

Q: What is your **diagnosis**?
A: Chronic myeloid leukaemia.

Q: What is the **cause** of abdominal discomfort?
A: Splenomegaly, which may be huge.

Q: What **investigation** do you suggest?
A: As follows:

- Bone marrow study.
- Cytogenetic analysis for Philadelphia chromosome.
- RNA analysis to see the presence of BCR–ABL gene product.
- Leukocyte alkaline phosphatase (LAP) score (decreases).

Q: What are the **therapies** that may cure this condition?
A: Bone marrow transplantation, imatinib and α-interferon.

N.B. In a middle-aged patient with huge splenomegaly and presence of anaemia, leucocytosis with myelocyte and metamyelocyte, few blasts, high basophil, high ESR is suggestive of chronic myeloid leukaemia (CML). Blastic crisis, myelofibrosis may occur. CML may be associated with low LAP score, high uric acid, high vitamin B_{12} and high LDH.

Case 03: Multiple Myeloma

A 65-year-old man presented with generalized body ache for the last 3 months. Laboratory investigation reveals:

- Hb 8 g/dL, WBC normal, platelet 2,00,000/cmm.
- ESR: 115 mm in 1st hour.
- PBF: Normocytic normochromic anaemia with increased rouleaux formation.
- Blood Ca^{++}: High.

Q: What is the likely **diagnosis**?
A: Multiple myeloma.

Q: Write down two important **investigations** to confirm the diagnosis.
A: As follows:

- Bone marrow study (shows atypical plasma cells).
- Serum protein electrophoresis or immunoelectrophoresis.
- X-ray skull (shows multiple lytic lesions).

Q: Write down three **complications**.
A: As follows:

- Pathological fracture of bone.
- Renal failure.
- Hyperviscosity syndrome.
- Bone marrow failure.
- Repeated infection.

Q: Mention one **drug** that may be curative.
A: Bortezomib.

N.B. Elderly patient may present with generalized bodyache, unexplained anaemia, repeated infection, spontaneous fracture, hyperviscosity syndrome, bleeding disorder, renal failure in multiple myeloma. Blood examination shows very-high ESR with marked rouleaux formation in peripheral blood film (PBF). Bone marrow study shows presence of atypical plasma cells (usually >20%). Urine shows Bence–Jones proteinuria.

Case 04: Pancytopaenia

A 40-year-old male presented with generalized weakness and gum bleeding for 2 months. Investigation reveals:

- Hb: 7 g/dL.
- WBC: 15,000/mm^3.
- Neutrophil: 16%.
- Lymphocyte: 81%.
- Platelet: 20,000/mm^3.
- ESR: 70 mm in 1st hour.

Q: What is the haematological **diagnosis**?
A: Pancytopaenia.

Q: Mention three **causes**.
A: As follows:

- Aplastic anaemia.
- Hypersplenism.
- Megaloblastic anaemia.
- Aleukaemic leukaemia.
- Paroxysmal nocturnal haemoglobinuria.

Q: Mention one **investigation** to confirm the diagnosis?
A: Bone marrow study.

N.B. Anaemia, leucopaenia and thrombocytopaenia indicates pancytopaenia. Commonest cause is aplastic anaemia. The causes of aplastic anaemia are—primary idiopathic, secondary (bone marrow infiltration, multiple myeloma, drugs, radiotherapy, etc.).

Case 05: Hypochromic Microcytic Anaemia

A 29-year-old female presented with weakness, palpitation and shortness of breath on exertion. Laboratory investigation reveals:

- Hb 8.5 mg/dL.
- RBC, WBC and platelet counts are within normal limits.
- PBF shows hypochromia.
- MCV 65 fL (normal >80 fL).

Q: What is haematological **diagnosis**?
A: Hypochromic microcytic anaemia.

Q: Mention four **causes**.
A: As follows:

- Iron-deficiency anaemia.
- β-Thalassaemia.
- Sideroblastic anaemia.
- Anaemia of chronic disorder.

Q: Which one is more likely **diagnosis** in this patient?
A: Iron-deficiency anaemia.

Q: What is the commonest **cause** of iron-deficiency anaemia?
A: Bleeding (menorrhagia, haemorrhoid).

Q: What **history** do you like to take in this female patient?
A: History of menorrhagia.

Q: What further **investigation** will you do?
A: As follows:

- Iron profile [serum iron, serum ferritin, total iron binding capacity (TIBC)].
- Haemoglobin electrophoresis.
- Bone marrow study.

N.B. Microcytic hypochromic blood picture with history of blood loss suggests iron-deficiency anaemia. Serum iron and ferritin will be low and TIBC will be high. Treatment includes correction of anaemia by blood transfusion, iron therapy for 3–6 months (to replenish the store) and treatment of primary cause.

Case 06: β-Thalassaemia Major

A 15-year-old girl presented with weakness, abdominal distension and loss of appetite. Examination of the abdomen reveals huge splenomegaly and mild hepatomegaly. Laboratory results show:

- Hb 7%, WBC 7200/cmm, neutrophil 62%, lymphocyte 23%, platelet 2,30,000/cmm.
- Reticulocyte: 10%.
- Mean cell volume (MCV): 69 fL (normal >80).
- Serum bilirubin: 3.1 mg/dL.

Q: What is the likely **diagnosis**?
A: β-Thalassaemia major.

Q: What is the **triad of signs** in this condition?
A: As follows:

- Anaemia.
- Jaundice.
- Splenomegaly.

Q: What **history** is important in such condition?
A: Family history of such illness.

Q: What **physical sign** will you look for?
A: Anaemia, jaundice, frontal and parietal bossing, mongoloid facies and splenomegaly.

Q: What **investigation** will you do to confirm the diagnosis?
A: Haemoglobin electrophoresis.

Q: How to **treat**?
A: As follows:

- Blood transfusion to keep the haemoglobin above 10 g/dL, usually every 4 months (life span of RBC is 4 months).
- Folic acid daily.
- Iron-containing drugs and diet should be avoided.
- Desferrioxamine to prevent transfusion haemosiderosis.
- Erythropoietin and hydroxyurea may be given.
- Specific treatment: Allogenic bone marrow transplantation.
- If huge splenomegaly with features of hypersplenism: Splenectomy may be done.

N.B. Presence of microcytic hypochromic anaemia with high reticulocyte count, jaundice and splenomegaly in a young patient indicates hereditary haemolytic anaemia, most commonly β-thalassaemia major. Other common hereditary haemolytic anaemia—HbE disease, thalassaemia E disease (double heterozygous).

Case 07: Macrocytic Anaemia

A 50-year-old woman presented with weakness and anorexia for 3 months. Her laboratory investigations reveal:

- Hb 8%, WBC 6700/cmm, neutrophil 65%, lymphocytes 25%, platelet 2,10,000/cmm.
- Reticulocyte: 1%.
- MCV: 112 fL (normal up to 96 fL).
- PBF shows macrocytosis and hypersegmented neutrophils.
- Serum bilirubin: 1.0 mg/dL.

Q: What is the haematological **diagnosis**?
A: Macrocytic anaemia.

Q: What are the **causes** of macrocytosis?
A: As follows:

- Megaloblastic anaemia (due to B_{12} or folic acid deficiency).
- Hypothyroidism.
- Chronic liver disease.
- Chronic alcoholism.
- Haemolysis.
- Azathioprine therapy.

Q: What next **investigation** should be done?
A: Bone marrow study.

Q: What are the **findings in bone marrow** study and how to interpret?
A: As follows:

- If macrocytosis is associated with megaloblast in bone marrow: The diagnosis is megaloblastic anaemia.
- If macrocytosis is associated with normoblastic bone marrow: The causes are hypothyroidism, chronic liver disease, chronic alcoholism, haemolysis, azathioprine therapy, etc.

Q: What other **investigations** do you suggest?
A: Serum vitamin B_{12} and folic acid assay.

N.B. Anaemia with high MCV indicates macrocytic anaemia. Most common cause is megaloblastic anaemia due to vitamin B_{12} or folic acid deficiency.

Case 08: Leukemoid Reaction

A 60-year-old man presents with fever, cough and weight loss. She was suffering from breast cancer, which was treated by mastectomy and chemotherapy. Her blood picture shows:

- Hb 11.4 g/dL, WBCs 23,700/cmm, polymorphs 82%, lymphocytes 6%, metamyelocytes 3%, myelocytes 3%, promyelocytes 1%, myeloblast 1%, erythroblast 4%, platelets 1,80,000/cmm.
- ESR: 10 mm in 1st hour.
- Chest X-ray: Absent left breast shadow.

Q: What is the haematological **diagnosis**?
A: Leukemoid reaction.

Q: What is the likely **cause**?
A: Bone marrow infiltration from carcinoma of breast.

Q: Mention one further **investigation** to confirm your diagnosis?
A: Bone marrow study.

N.B. Leukemoid reaction means that the peripheral blood picture resembles leukaemia; but there is no leukaemia. It may be myeloid or lymphatic. Causes of myeloid leukemoid reaction are—leukoerythroblastic anaemia, infection, malignancy, acute haemolysis (LIMA). Causes of lymphatic leukemoid reaction: viral (infectious mononucleosis, cytomegalovirus infection, measles, chicken pox), whooping cough. Rarely, tuberculosis and carcinoma.

Case 09: Leukoerythroblastic Anaemia

A 65-year-old woman presented with pain in the epigastrium, loss of appetite, fever, generalized bodyache, night sweating, occasional headache, dizziness and weight loss for 3 months. She is pale and emaciated. There is massive splenomegaly. Investigations reveal:

- Hb 9.1 g/dL, WBC 18,500/cmm, polymorphs 60%, lymphocytes 28%, myelocytes 6%, metamyelocytes 2%, myeloblasts 1%, erythroblast 3%, ESR 93 mm in 1st hour, platelets 6,65,000/cmm.
- Liver function tests: Serum bilirubin 28 µmol/L, SGPT 38 IU/L, alkaline phosphatase 200 IU/L.
- Chest X-ray: Normal.

Q: What is the haematological **diagnosis**?
A: Leukoerythroblastic anaemia.

Q: What is the likely **diagnosis**?
A: Myelofibrosis.

Q: What additional findings may be seen in **blood film**?
A: Tear-drop poikilocytes.

Q: What are the other **causes** of such blood picture?
A: As follows:

- Secondary deposits in bone marrow.
- Lymphoma.

- Multiple myeloma.
- Active haemolytic anaemia.

Q: Suggest two other tests.
A: As follows:

- Bone marrow study: May be dry tap. Trephine biopsy is needed, which shows increased megakaryocyte, increased reticulin and fibrous tissue.
- LAP score: High.

Q: Mention one dangerous complication.
A: Transform to acute myeloid leukaemia (AML) (10–20% cases).

Q: What treatment should be given?
A: As follows:

- Blood transfusion.
- Folic acid.
- Hydroxycarbamide (hydroxyurea) may be given.
- In young patient, bone marrow transplantation.
- Radiotherapy for huge spleen.
- If evidence of hypersplenism and huge spleen with pressure symptoms, splenectomy may be necessary.

N.B. In any elderly patient with huge splenomegaly and leukoerythroblastic blood picture, the likely cause is myelofibrosis. PBF shows tear-drop or pear-drop poikilocytes. Myelofibrosis is a disorder of unknown cause, characterized by bone marrow fibrosis, extramedullary haemopoiesis and leukoerythroblastic blood picture due to neoplastic proliferation of primitive stem cells. It is common above 50 years. There may be peptic ulcer, pruritus after hot bath, gout, etc.

Case 10: Blastic Crisis in Chronic Myeloid Leukaemia (CML)

A 53-year-old man is diagnosed as a case of chronic granulocytic leukaemia. He was treated with chemotherapy and responded well. Three years later, the patient presented with the complaints of severe weakness, loss of weight, lethargy, epistaxis and pain in left upper abdomen. Investigations show:

- Hb 7.5 g/dL, WBC 12,800/cmm, platelets 1,00,000/cmm, RBC 2.8 million/cmm, ESR 85 mm in 1st hour.
- Differential count: Neutrophils 34%, basophil 8%, lymphocyte 6%, myeloblast 40%, myelocyte 10%, metamyelocyte 2%.

Q: What is the diagnosis?
A: Blastic crisis in CML

Q: What is the cause of abdominal pain?
A: Splenic infarction.

Q: Suggest one investigation to confirm your diagnosis.
A: Bone marrow study.

N.B. Appearance of increased number of blast cells in PBF in a patient with CML suggests blastic crisis. It may be myeloid or lymphatic.

Case 11: Idiopathic Thrombocytopenic Purpura

9 days after recovering from a viral fever, a 13-year-old girl presents with several small bruises on her arms and legs. Investigations reveal:

- Full blood count: Hb 11.3 g/dL, WBCs 10,700/cmm, polymorphs 59%, lymphocytes 38%, ESR 60 mm in 1st hour. Platelet count 80,000/cmm.
- Blood film: Normocytic and normochromic.
- Chest X-ray: Normal.

Q: What is the likely diagnosis?
A: Idiopathic thrombocytopenic purpura.

Q: Suggest two diagnostically useful investigations.
A: Bone marrow study, antiplatelet antibody.

Q: What disease should be excluded in such finding?
A: Systemic lupus erythematosus (SLE).

Q: What treatment should be given?
A: In child—usually self-limiting. If no improvement:

- Prednisolone (2 mg/kg)
- If persistent bleeding, I/V immunoglobulin.
- Platelet transfusion, if persistent bleeding.
- If thrombocytopaenia persists for more than 6 months, it is chronic. In that case, splenectomy should be considered.

N.B. Purpuric spot in a patient with recent history of viral fever, associated with low platelet count and increased megakaryocytes in bone marrow is suggestive of idiopathic thrombocytopenic purpura (ITP). In ITP, low platelet, increased megakaryocyte in bone marrow, prolonged bleeding time, normal clotting time are common. There may be antiplatelet antibody and anticardiolipin antibody. Initially, SLE and antiphospholipid syndrome may present like ITP.

Case 12: Polycythemia Rubra Vera

A 41-year-old man presented with frequent headache, dizziness, lack of concentration, pruritus and heaviness in the left upper abdomen for 3 months. Laboratory investigations reveal:

- Hb 17.6 g/dL, WBCs 21,000/cmm, polymorphs 83%, lymphocytes 15%, eosinophils 2%, RBCs 8.2 million/cmm, platelets 8,50,000/cmm, ESR 1 mm in 1st hour.
- Packed cell volume (PCV): 65% (normal up to 45%).
- Random blood sugar (RBS): 7.2 mmol/L.
- Chest X-ray: Normal.

Q: What is your **diagnosis**?
A: Polycythemia rubra vera (PRV).

Q: Suggest one **investigation**.
A: Measurement of red cell mass (increased).

Q: Suggest one **treatment**.
A: Venesection.

Q: What **drugs** can be used?
A: Radioactive phosphorus, hydroxyurea, interferon.

Q: Mention four **complications**.
A: As follows:

- AML.
- Thromboembolism (cerebral, coronary).
- Hypertension.
- Gout.
- Peptic ulcer.
- Myelofibrosis.

N.B. This patient has high haemoglobin and RBC, also high PCV, which suggests polycythaemia. High WBC and platelet count associated with splenomegaly are all in favour of polycythemia rubra vera. Red cell volume is high in PRV. There is increased LAP (leukocyte alkaline phosphatase), vitamin B_{12} and uric acid (may cause gout). Bone marrow shows hypercellular with increased megakaryocyte.

Case 13: Disseminated Intravascular Coagulation (DIC)

A 29-year-old woman was admitted in the hospital with the complaints of PV (blood loss per vaginum) bleeding and high grade, continuous fever, following a self-induced abortion. She looks toxic, anaemia – severe, BP 80/60 mmHg, pulse 124/min, temperature 39.6°C. Lower abdomen – very tender. Investigations reveal:

- Full blood count: Hb 5.0 g/dL, WBCs 28,700/cmm, polymorphs 87%, lymphocytes 13%, platelets 30,000/cmm, ESR 85 mm in 1st hour.
- PBF: Microcytic, hypochromic and fragmented RBC.
- Prothrombin time: 30 s (control 12).
- APTT: 60 s (control 32).
- Fibrinogen: 0.05 g/L (1.5–4.0 g).

Q: What is the main **diagnosis** in this blood disorder?
A: Disseminated intravascular coagulation (DIC).

Q: Mention four **abnormalities** in this blood picture.
A: DIC with microangiopathic haemolytic anaemia with iron-deficiency anaemia along with septicaemia.

Q: Give three possible **causes** of haematological abnormality.
A: Septicaemia, retained product of conception or amniotic fluid embolism.

N.B. DIC is a haemorrhagic disorder in which diffuse intravascular clotting causes a haemostatic defect resulting from utilization of coagulation factor and platelet in the clotting process. There is secondary activation of fibrinolysis, leading to production of fibrin degradation products (FDP). The consequence of these changes is a mixture of initial thrombosis, followed by bleeding tendency due to consumption of coagulation factors and fibrinolytic activity.

Respiratory

Case 01: Interstitial Lung Disease

A 46-year-old woman is admitted in the emergency department with shortness of breath, cough, swelling in both feet and extreme weakness. Respiratory function tests reveal:

- Vital capacity: 2.0 L (predicted 2.4–3.6 L).
- FEV_1: 2.1 L (predicted 2.25–3.25 L).
- Transfer factor: 4.1 L (predicted 5.8–8.7 L).
- Residual volume: 1.1 L (predicted 1.55–2.32 L).

Q: What pulmonary **defect** is present?
A: Restrictive lung disease.

Q: What is the likely **diagnosis** with the above findings?
A: Interstitial lung disease.

Q: Suggest five **investigations** to find out cause.
A: As follows:

- Chest X-ray.
- CT scan of chest.
- ABG (arterial blood gas) analysis.
- Bronchoscopy and bronchoalveolar lavage.
- Transbronchial or open lung biopsy.

Q: What are the **causes** of restrictive lung disease?
A: As follows:

- Sarcoidosis.
- DPLD.
- Ankylosing spondylitis.

N.B. In restrictive lung disease, both FVC and FEV_1 are proportionately reduced; but ratio of this two is normal. Total lung capacity is reduced and residual volume is reduced or normal. CO transfer factor is also low.

Case 02: Emphysema

A lady of 42 years, housewife, has been suffering from breathlessness, occasional dry cough and weight loss for 2 years. Her lung function test shows:

- FVC: 2.00 L (predicted 2.4–3.6 L).
- FEV_1: 1.45 L (predicted 2.25–3.25 L).
- RV: 2.89 L (predicted 1.5–2.32 L).
- FRC: 3.56 L (predicted 2.17–3.25 L).
- TLC: 5.89 L (predicted 3.96–5.66 L).
- TLCO: 4.7 mmol/min/kPa (predicted 5.8–8.7 L).

Q: What is the **lung function test**?
A: Obstructive airway disease.

Q: What is the most likely **diagnosis**?
A: Emphysema.

Q: Suggest two possible **causes**.
A: α_1-Antitrypsin deficiency, cigarette smoking.

Q: **Name** two obstructive airway disease.
A: Chronic obstructive pulmonary disease (COPD), bronchial asthma.

N.B. In obstructive lung disease, forced expiratory volume in 1 second (FEV_1) is markedly reduced; forced vital capacity (FVC) is also reduced. The ratio of these two is also reduced. CO transfer factor is low. Residual volume and total lung capacity are high.

Endocrine

Case 01: Primary Hyperparathyroidism

A 52-year-old woman presented with frequency of micturition, extreme weakness, loss of appetite, constipation, abdominal pain and weight loss for 7 months. Investigations reveal:

- Full blood count: Hb 10.6 g/dL, WBCs 8,900/cmm, polymorphs 55%, lymphocytes 43%, monocytes 2%, ESR 90 mm in 1st hour.
- Plain X-ray KUB (kidneys, ureters, bladder): Nephrocalcinosis.
- USG of abdomen: Calcification in both kidneys.
- Urine: Protein (+), few pus cells.
- RBS: 6.9 mmol/L.
- Creatinine: 1.4 mg/dL.
- Serum electrolytes: Sodium 139 mmol/L, chloride 110 mmol/L, potassium 3.6 mmol/L, bicarbonate 22 mmol/L.

Q: What is the likely **diagnosis**?
A: Primary hyperparathyroidism.

Q: Suggest **five investigations** to confirm your diagnosis.
A: As follows:

- Serum calcium, phosphate and alkaline phosphatase.
- Parathormone assay.
- Hydrocortisone suppression test.
- X-ray of hand (to see subperiosteal erosion in the medial side of phalanges) and X-ray of skull (to see pepper-pot appearance).
- USG or CT scan of neck (parathyroid adenoma or hyperplasia).
- Other test: Thallium/technetium subtraction scan of thyroid and parathyroid.

Q: What single **treatment** should be given immediately?
A: Plenty of fluid (infusion of normal saline 4–6 L daily) for hypercalcaemia.

N.B. The above symptoms associated with hypercalcaemia and nephrocalcinosis indicates hyperparathyroidism. It may be primary (due to adenoma, hyperplasia or carcinoma of parathyroid), secondary (chronic renal failure, malabsorption, rickets or osteomalacia) or tertiary (autonomous from secondary). In mild and asymptomatic case follow-up. Total parathyroidectomy with transplantation of parathyroid in the forearm muscles is done in primary hyperparathyroidism. Surgery is also required for tertiary hyperparathyroidism. Treatment of secondary causes should be done.

Case 02: Thyrotoxicosis due to Graves Disease

A 32-year-old lady presented with bilateral proptosis, gritty sensation and discomfort in both eyes, palpitation and weight loss. Investigation reveals:

- Serum FT_3: 9.0 pmol/L (normal 1.3–3.5 pmol/L).
- Serum FT_4: 215 pmol/L (normal 70–160 pmol/L).
- TSH: 0.04 mIU/L (normal 0.5–5.1 mIU/L).

Q: What is your **diagnosis**?
A: Thyrotoxicosis due to Graves disease.

Q: Write down two other **causes** of such investigation findings.
A: As follows:

- Toxic multinodular goitre.
- Toxic adenoma.

Q: Write down **two important finding** by examining the nervous system of this patient.
A: As follows:

- Tremor of the outstretched hand.
- Jerks are exaggerated

Q: Write down four other important **investigations**.
A: As follows:

- Radio-iodine uptake test.
- Thyroid scan.
- USG of neck.
- TSH receptor antibody (TRAb) test.

Q: Write down the modalities of **treatment**.
A: As follows:

- Antithyroid drugs: Carbimazole or propylthiouracil.
- Radioactive iodine therapy.
- Thyroid surgery.

N.B. Graves disease is characterized by diffuse goitre, exophthalmos and dermopathy. The natural history of Graves disease is hyperthyroidism, followed by euthyroid and later, hypothyroidism. TSH receptor antibody (TRAb) is high. Antimicrosomal (antiperoxidase) and antithyroglobulin antibody may be present in low titre.

Case 03: Primary Hypothyroidism

A 35-year-old female presented with generalized weakness and weight gain. Her thyroid function test reveals:

- Serum FT_3: 2 pmol/L (normal 1.3–3.5 pmol/L).
- Serum FT_4: 7 pmol/L (normal 70–160 pmol/L).
- TSH: 35 mIU/L (normal 0.5–5.1 mIU/L).

Q: What is the most likely clinical **diagnosis**?
A: Primary hypothyroidism.

Q: Mention four important **clinical signs** of this patient.
A: As follows:

- Hoarseness or croaky voice.
- Puffiness of face.

- Bradycardia.
- Delayed relaxation of ankle jerk.

Q: What are the ECG changes in hypothyroidism?
A: As follows:

- Sinus Bradycardia.
- Low-voltage ECG tracing.
- T-wave inversion.

Q: What is the **treatment**?
A: Lifelong thyroxine replacement, starting with low dose (25 microgram/day) and then gradually increasing the dose.

N.B. Weight gain, increased sleepiness, cold intolerance and constipation are the usual features of hypothyroidism. Polyserositis may occur in myxoedema. Muscular pain, arthralgia, effusion in any serous cavity may occur. SIADH, high creatinine phosphokinase (CPK), serum glutamic pyruvic transaminase (SGPT), serum glutamic oxaloacetic transaminase (SGOT), lactic dehydrogenase (LDH) may also be found.

Case 04: Sick Euthyroid Syndrome

A 65-year-old, obese woman is hospitalized with the complaints of fever, cough with purulent sputum for 3 days. Investigations reveal:

- Full blood count: Hb 10.5 g/dL, WBCs 18,540/cmm, polymorphs 82%, lymphocytes 16%, monocytes 2%, platelets 1,80,000/cmm.
- Chest X-ray: Consolidation (left upper zone).
- ECG: Low-voltage tracing and sinus bradycardia.
- Serum FT_3: 2.2 pmol/L (normal 1.3–3.5 pmol/L).
- Serum FT_4: 104 pmol/L (normal 70–160 pmol/L).
- TSH: 0.2 mIU/L (normal 0.5–5.1 mIU/L).

Q: What is the likely **diagnosis** of thyroid disorder?
A: Sick euthyroid syndrome.

Q: What further **investigation** would you suggest?
A: Repeat FT_3, FT_4 and TSH after cure of pneumonia.

Q: What is the **cause** of ECG abnormality?
A: Obesity.

N.B. In any extrathyroidal illness [acute myocardial infarction, pneumonia, cardiovascular disease (CVD)], there may be abnormal thyroid function tests; although the patient is euthyroid. This is called sick euthyroid syndrome. There may be low total and free T_3 and T_4 along with low or normal thyroid stimulating hormone (TSH). It is confused with secondary hypothyroidism. The tests should be repeated after recovery from the systemic disease, usually after 6 weeks.

Case 05: de Quervain Thyroiditis

A 32-year-old woman presents with fever, dry cough, pain in the throat, headache, bodyache, palpitation and intolerance to heat for 1 week. There is fine tremor of the outstretched hands. Palms are warm and sweaty. Thyroid is diffusely enlarged, soft, nontender, no bruit. Investigations reveal:

- Full blood count: Hb 11.1 g/dL, WBCs 3,500/cmm, polymorphs 48%, lymphocytes 52%, ESR 110 mm in 1st hour, platelets 3,65,000/cmm.
- Chest X-ray: Normal.
- Serum FT_3: 8.7 pmol/L (normal 1.3–3.5 pmol/L).
- Serum FT_4: 205 pmol/L (normal 70–160 pmol/L).
- TSH: 0.4 mIU/L (normal 0.5–5.1 mIU/L).
- Radio-iodine uptake: After 2 h, 7% (normal 5–15%). After 24 h, 5.1% (normal 15–30%).

Q: What is the likely **diagnosis**?
A: de Quervain thyroiditis (subacute thyroiditis).

Q: Suggest one **investigation**.
A: Fine-needle aspiration cytology (FNAC) of thyroid gland.

Q: Mention three other **causes** of such thyroid functions (high T_3, T_4 but low radio-iodine uptake).
A: As follows:

- Postpartum thyroiditis.
- Factitious hyperthyroidism.
- Iodine-induced hyperthyroidism.

N.B. de Quervain thyroiditis is a virus-induced transient inflammation of thyroid gland, usually self-limiting. It is caused by Coxsackie B4, also may be associated with influenza, infectious mononucleosis, measles, mumps, common cold. It is more in females, 20–40 years. Presents with pain over thyroid, radiate to jaw, ear, and gets worse by coughing, swallowing or movement of neck. Systemic features are common. Thyroid gland is enlarged and tender. FNAC shows presence of giant cells. ESR is typically high. Inflammation of thyroid releases thyroid hormones, which are high in the blood, responsible for the features of thyrotoxicosis. This may persist for 4–6 weeks. Iodine uptake is low. Hyperthyroidism followed by transient hypothyroidism may occur. Complete recovery occurs in 4–6 months. Treatment: Symptomatic (NSAID). Propranolol may be used. Prednisolone 40 mg/day for 3–4 weeks may be needed. Antithyroid drug should not be given.

Case 06: Euthyroid State

A young lady with 4 months' pregnancy presented with the complaints of palpitation, excessive sweating and intolerance to heat. Thyroid gland is diffusely enlarged and nontender, soft. Investigation reveals:

- Full blood count: Hb 10.5 g/dL, WBCs 9,800/cmm, polymorphs 66%, lymphocytes 30%, eosinophils 4%, platelets 2,00,000/cmm, ESR 85 mm in 1st hour.
- Serum T_4: 290 nmol/L (normal 70–160 nmol/L).
- Serum T_3: 9 nmol/L (normal 1.32–3.1 nmol/L).
- Serum TSH: 4 mIU/L (normal 1.52–5 mIU/L).

Q: What is your **inference** from the above result?
A: Euthyroid state.

Q: What further **investigations** should be done?
A: FT_3 and FT_4.

Q: Mention **four causes** of such thyroid function abnormality.
A: Pregnancy, oral contraceptive pill, oestrogen therapy, acute intermittent porphyria.

N.B. Patient's symptoms are due to pregnancy. Thyroid gland may be normally enlarged in pregnancy, so her total T_3 and T_4 are high, but TSH is normal.

Any causes of high thyroxine-binding globulin (TBG) will also cause high T_3 and T_4, but FT_3 and FT_4 will be normal. Alternately, any cause of low TBG will also cause low T_3 and T_4.

Causes of high TBG: Congenital or hereditary, pregnancy, drug (oestrogen, clofibrate, phenothiazine), oral contraceptive pills, acute intermittent porphyria, acute viral hepatitis; also in hypothyroidism.

Causes of low TBG: Hereditary, malnutrition, nephrotic syndrome, liver failure, drugs (sulphonylurea, salicylate, phenytoin, phenylbutazone, anabolic steroid, androgen, corticosteroid), active acromegaly. Also in hyperthyroidism.

Case 07: Cushing Syndrome

A housewife of 40 years, presented with frequent headache, vertigo and insomnia for 2 months. Blood pressure (BP) is 160/100 mmHg. Investigations reveal:

- Full blood count: Hb 11.5 g/dL, WBCs 8300/cmm, polymorphs 64%, lymphocytes 33%, monocytes 3%, ESR 48 mm in 1st hour, platelets 2,70,000/cmm.
- Urine: Glycosuria (++), proteinuria (+).
- Serum electrolytes: Sodium 145 mmol/L, chloride 101 mmol/L, potassium 3.1 mmol/L, bicarbonate 30 mmol/L.
- Creatinine: 1.3 mg/dL.
- Chest X-ray: Heart slightly enlarged.
- Fasting blood sugar (FBS): 9.0 mmol/L.

Q: Suggest three **differential diagnoses**.
A: Cushing syndrome, primary aldosteronism, ectopic adrenocorticotropic hormone (ACTH) syndrome.

Q: What is the **likely diagnosis** in this case?
A: Cushing syndrome.

Q: What **five physical signs** will you see?
A: Obesity, striae, plethoric face, skin is thin with bruise, proximal myopathy.

Q: Mention **four further investigations**.
A: As follows:

- Serum morning and midnight cortisol.
- Dexamethasone suppression test.
- Ultrasonography of abdomen (to see suprarenal gland).
- CT scan or MRI of suprarenal glands.

N.B. Hypertension with hypokalaemia and diabetes mellitus is highly suggestive of Cushing syndrome. In primary aldosteronism, diabetes mellitus is not common and hypokalaemia is more severe. To diagnose Cushing syndrome, serum morning and midnight cortisol, 24 h urinary-free cortisol, short overnight dexamethasone suppression test should be done, to see whether Cushing syndrome is present or not. Then further test should be done to find out causes (e.g. ACTH, X-ray chest, USG of suprarenal gland, CT or MRI of suprarenal glands and pituitary gland).

Case 08: Primary Hyperaldosteronism

A 25-year-old female is complaining of excessive thirst, weakness, polyuria, nocturia and insomnia for 6 months. Her BP is 165/115 mmHg. Investigations reveal:

- Full blood count: Hb 12.7 g/dL, WBCs 6800/cmm, polymorphs 60%, lymphocytes 39%, monocytes 1%, ESR 20 mm in 1st hour.
- Urea: 38 mg/dL (normal 9–11 mg/dL).
- Creatinine: 1.2 mg/dL (normal 0.68–1.36 mg/dL).
- Serum electrolytes: Sodium 148 mmol/L, chloride 107 mmol/L, potassium 2.8 mmol/L, bicarbonate 32 mmol/L.
- RBS: 9.3 mmol/L.
- Chest X-ray: Cardiomegaly, left ventricular type.

Q: What is your **diagnosis**?
A: Primary hyperaldosteronism.

Q: Suggest three **investigations** to confirm your diagnosis.
A: As follows:

- Serum aldosterone and rennin assay.
- 24-h urine potassium.
- CT scan or MRI of adrenal glands.

N.B. Hypertension with hypokalaemic alkalosis is highly suggestive of primary hyperaldosteronism; it is also called Conn syndrome. It is an aldosterone-secreting tumour responsible for <1% cause of hypertension. Excess aldosterone secretion leads to sodium retention, hypokalaemia and hypertension. It is due to adrenal adenoma in 60% (Conn syndrome) and 30% bilateral adrenal hyperplasia. Serum renin is low in primary aldosteronism, whereas renin is high in secondary aldosteronism. *Treatment:* If adenoma, surgery. If hyperplasia, spironolactone 100–400 mg daily. For hypertension, amiloride and calcium channel blocker may be used.

Case 09: Hypokalaemic Metabolic Alkalosis

A 45-year-old female presented with blood pressure of 170/100 mmHg. Investigation reveals:

- Na^+: 156 mmol/L.
- K^+: 2.5 mmol/L.
- Cl^-: 102 mmol/L.
- HCO_3^-: 30 mmol/L.

Q: What are the **abnormalities** in the investigations?
A: As follows:

- Hypernatraemia.
- Hypokalaemia.
- Metabolic alkalosis.

Q: Name three possible **causes** of this investigation finding.
A: As follows:

- Cushing syndrome.
- Conn syndrome (primary hyperaldosteronism).
- Renal artery stenosis.

Q: Name four other **investigation** to confirm the diagnosis.
A: As follows:

- Plasma cortisol.
- Urinary free cortisol.
- Plasma rennin and aldosterone assay (to see the ratio).
- USG of kidney and adrenal gland.
- CT or MRI of suprarenal gland.

Case 10: Addison Disease

A 22-year-old man was admitted with the complaints of weakness and weight loss for several weeks. His blood pressure is 80/50 mmHg. Investigations reveal:

- Na^+: 122 mmol/L.
- K^+: 6.3 mmol/L.
- Cl^-: 98 mmol/L.
- HCO_3^-: 20 mmol/L.

Q: What are the biochemical **abnormalities**?
A: As follows:

- Hyponatraemia.
- Hyperkalaemia.
- Acidosis.

Q: What is the likely **diagnosis**?
A: Addison disease.

Q: Mention one important **clinical sign**.
A: Pigmentation of skin and mucous membrane.

Q: What are the common causes?
A: As follows:

- Autoimmune.
- Tuberculosis.

Q: Name other four **investigations** to confirm the diagnosis.
A: As follows:

- Plasma cortisol and ACTH level.
- Synacthen test.
- USG of kidney and suprarenal gland.
- Plain X-ray abdomen (to see suprarenal calcification).

N.B. In any patient with weakness, hypotension, pigmentation associated with low sodium and high potassium is highly suggestive of Addison disease. It is the primary adrenocortical insufficiency due to destruction of adrenal gland, resulting in deficiency in glucocorticoid and mineralocorticoid. Supine BP may be normal; but marked drop of systolic pressure on standing may occur. There will be low serum cortisol and high ACTH. Short Synacthen test is helpful for diagnosis. Treatment: Hydrocortisone should be given, mineralocorticoid may be necessary. Steroid card should be maintained.

Case 11: Diabetic Ketoacidosis

A 19-year-old woman was suffering from high-grade fever, productive cough, shortness of breath, diffuse abdominal pain and vomiting. She is emaciated and dehydrated. Investigations reveal:

- Blood glucose: 28 mmol/L.
- Serum electrolytes: Na 118 mmol/L, potassium 4.7 mmol/L, chloride 98 mmol/L and bicarbonate 8.1 mmol/L.
- Serum creatinine: 1.1 mg/dL

Q: What is the likely **diagnosis**?
A: Diabetic ketoacidosis (DKA).

Q: What other **investigations** should be done?
A: Urine for ketone bodies.

Q: What are the **complications**?
A: As follows:

- Acute respiratory distress syndrome.
- Thromboembolism.
- DIC.
- Acute renal failure.
- Cerebral oedema.

N.B. Dry tongue, weight loss, high blood sugar with severe metabolic acidosis indicates DKA. It is common in type 1 diabetes mellitus. Three main problems in DKA are: (i) hyperglycaemia, (ii) hyperketonaemia and (iii) metabolic acidosis. Marked dehydration is common. Five percent cases develop coma in DKA. If bicarbonate is <12 mmol/L, it indicates severe acidosis.

Treatment: Intravenous (IV) normal saline rapidly, IV soluble insulin preferably with pump, potassium therapy, control of infection, correction of acidosis by isotonic 1.26% soda bicarb, if arterial pH is <7 (complete correction of acidosis is avoided because there is correction of extracellular acidosis, but acidosis in brain is persistent, which aggravates cellular dysfunction in brain). Mortality is 5–10%, more in elderly.

Case 12: Hyperosmolar Nonketotic Diabetic Coma with Urinary Tract Infection (UTI)

A 70-year-old lady was suffering from fever and frequency of micturition for 10 days. She became unconscious for the last 2 h. BP 90/60 mmHg, pulse 110/min, marked dehydration. Investigations reveal:

- Full blood count: Hb 11.2 g/dL, WBCs 17,000/cmm, polymorphs 85%, lymphocytes 15%, platelets 2,10,000/cmm, ESR 12 mm in 1st hour.
- Serum electrolytes: Sodium 162 mmol/L, chloride 110 mmol/L, potassium 4.6 mmol/L, bicarbonate 22 mmol/L.
- Serum creatinine: 1.4 mg/dL.
- Urine: Plenty of pus cells, albumin (++), glucose (+++).
- Chest X-ray: Normal.
- CT scan of brain: Diffuse age-related cerebral atrophy.

Q: What is the likely **diagnosis**?
A: Hyperosmolar nonketotic diabetic coma with urinary tract infection (UTI).

Q: Suggest two **investigations**.
A: As follows:

- RBS.
- Urine for ketone bodies.

Q: What immediate **therapeutic** measures would you start?
A: As follows:

- IV half-strength saline (0.45%).
- Soluble insulin (preferably with insulin pump, 2–6 units hourly).
- When osmolality is normal, 0.9% normal saline should be given.
- Other treatment: Nasogastric (NG) tube feeding, catheter if needed, antibiotic if infection, correction of electrolytes, low-dose heparin (as thrombosis is common).

N.B. Hyperosmolar nonketotic diabetic coma (HNDC) may be the first presentation in diabetes mellitus. Common in elderly, Noninsulin-dependent diabetes mellitus (NIDDM), characterized by very-high blood glucose (>50 mmol/L) and high plasma osmolality. No ketosis because insulin deficiency is partial and low insulin is present, which is sufficient to prevent ketone body formation, but insufficient to control hyperglycaemia. Precipitating factors are large amount of sweet drinks, infection, steroid, thiazide, myocardial infarction, etc. Plasma sodium is usually high. There may be high blood urea nitrogen (BUN); urea, creatinine and serum osmolality may be very high. Mortality rate may be up to 40%.

Case 13: Impaired Glucose Tolerance

This is the glucose tolerance test (GTT) report of a 46-year-old woman:

- FBS: 5.1 mmol/L.
- After 0.5 h: 7.6 mmol/L.
- After 1 h: 8.3 mmol/L.
- After 1.5 h: 10.6 mmol/L.
- After 2.0 h: 10.1 mmol/L.

Q: What is the **glycaemic status**?
A: Impaired glucose tolerance (IGT).

Q: What does it **indicate**?
A: The patient is at high risk of developing type 2 diabetes mellitus.

N.B. When fasting glucose is <7 mmol, but during oral glucose tolerance test (OGTT), blood glucose is 7.8–11.0 mmol/L, 2 h after glucose load, it is called impaired glucose tolerance (IGT). This patient has increased risk of developing frank diabetes mellitus (DM) type 2 with time and macrovascular (cardiovascular) diseases are more. Lifestyle modification for type 2DM and annual check-up for glucose are recommended for the patient. Cardiovascular risk factors should be treated aggressively.

Case 14: Renal Glycosuria

A young patient during routine check-up presents with the following laboratory investigation:

- CBC: Normal.
- Urine R/E: Albumin nil, glucose ++, few epithelial cells, RBCs nil, pus cells nil.
- Blood glucose: 5.5 mmol/L.

Q: What is the **diagnosis**?
A: Renal glycosuria.

Q: What is the **prognosis**?
A: It is a benign disease.

N.B. Renal glycosuria is due to low renal threshold for glucose. Blood glucose level is normal. It is the most common cause of glycosuria and often found in pregnancy and young individuals. It is usually asymptomatic and rarely may lead to polyuria and polydipsia.

CHAPTER 14

X-Ray, CT and MRI

"Treat the patient, not the x-ray"

–James M. Hunter

Pleural Effusion

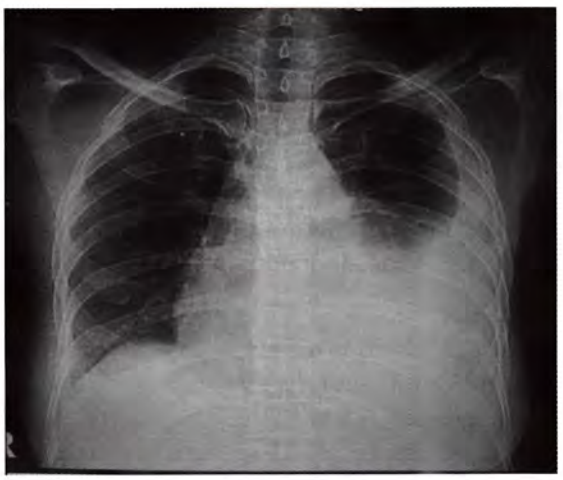


Fig. A: Left-sided pleural effusion

Q: Write down the radiological **findings** of the X-ray shown in Figure A.

A: X-ray chest PA view showing:

- Dense homogenous opacity in left lower zone with a curvilinear upper border.
- There is obliteration of left costophrenic angle.
- Trachea and heart (mediastinum) are shifted to the right.

Q: What is your radiological **diagnosis**?

A: Left-sided pleural effusion.

Q: Write down **one percussion and two auscultatory findings** of chest.

A: As follows:

- Percussion note stony dull.
- On auscultation: Diminished or absent breath sound and diminished or absent vocal resonance.

Q: Write down four common **causes**.

A: As follows:

- Pulmonary tuberculosis (TB).
- Parapneumonic.
- Bronchial carcinoma.
- Pulmonary infarction.

Q: Write down other **investigations** to confirm the diagnosis.

A: As follows:

- Complete blood count (CBC) with erythrocyte sedimentation rate (ESR).
- Tuberculin test.
- Pleural fluid analysis [physical character, cytology, biochemistry, Gram (Gm) stain, culture, acid fast bacilli (AFB), malignant cell, adenosine deaminase (ADA)].
- Pleural biopsy.
- Bronchoscopy and biopsy (if needed in bronchial carcinoma).



Fig. B: Bilateral pleural effusion

Q: Write down the radiological **findings** of the X-ray shown in Figure B.

A: X-ray chest PA view showing dense homogenous opacity with curvilinear upper border in both lower zones obliterating both costophrenic angles.

Q: What is your radiological **diagnosis**?

A: Bilateral pleural effusion.

Q: What are the **causes**?

A: As follows:

- Cirrhosis of liver.
- Nephrotic syndrome.
- Congestive cardiac failure.
- Bilateral extensive tuberculosis.
- Collagen disease: Systemic lupus erythematosus (SLE), rheumatoid arthritis.

Q: Write down the radiological **findings** of the X-ray shown in Figure C.

A: X-ray chest right decubitus view showing dense homogenous opacity in peripheral part of the chest with clear upper border.

Q: What is your radiological **diagnosis**?

A: Right-sided pleural effusion.

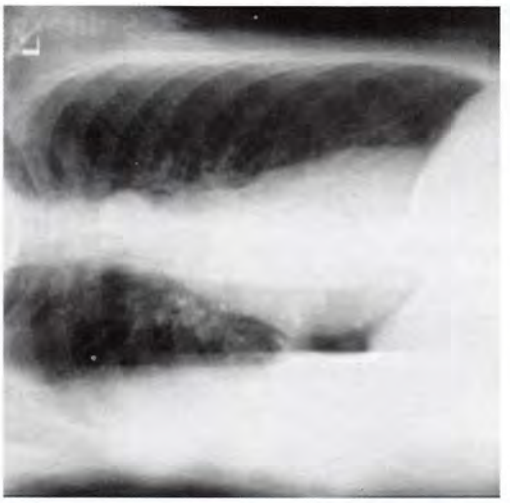


Fig. C: Right-sided pleural effusion (decubitus view)

Mass Lesion

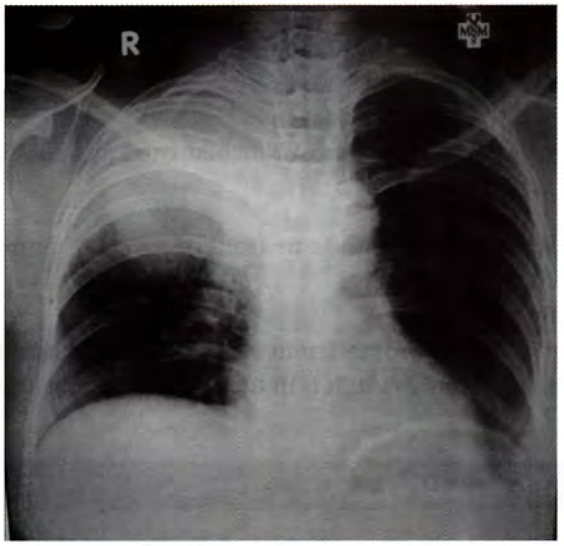


Fig. A: Mass lesion (bronchial carcinoma) in right lung

Q: Write down the radiological **finding** of the X-ray shown in Figure A.

A: X-ray chest PA view showing opacity with irregular margin, occupying the right upper and part of mid zone.

Q: What is your radiological **diagnosis**?

A: Bronchial carcinoma.

Q: Mention two **differential** diagnoses.

A: As follows:

- Tuberculosis.
- Consolidation.

Q: Mention three **investigations** to confirm your diagnosis?

A: As follows:

- Sputum for malignant cells (exfoliative cytology).
- CT- or ultrasonography-guided fine-needle aspiration cytology (FNAC).
- Bronchoscopy and biopsy.
- If palpable lymph node, then FNAC or biopsy.



Fig. B: Bronchial carcinoma with left phrenic nerve palsy

Q: Write down the radiological **finding** of the X-ray shown in Figure B.

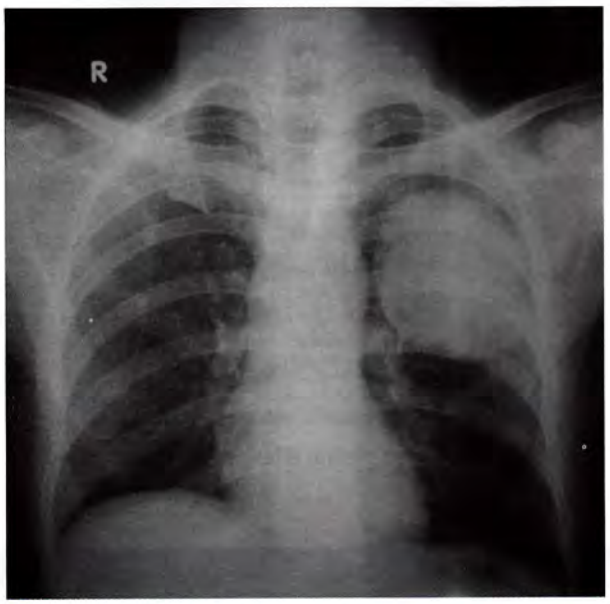
A: X-ray chest PA view showing:

- Opacity with irregular margin in the left upper and part of mid zones.
- Left dome of the diaphragm is raised.

Q: What is your radiological **diagnosis**?

A: Bronchial carcinoma with left phrenic nerve palsy.

Solitary Pulmonary Nodule



Left-sided solitary pulmonary nodule

Q: Write down the radiological **finding** of this X-ray.

A: Chest X-ray (CXR) PA view showing a homogeneous, rounded, nodular shadow with clear margin in left midzone.

Q: Mention five **causes**.

A: As follows:

- Consolidation.
- Tuberculoma.
- Bronchial carcinoma.
- Secondary deposit.
- Bronchial adenoma.
- Lung abscess before burst.
- Hydatid cyst.

N.B. Others causes are encysted pleural effusion, hamartoma, rheumatoid nodule, Wegener granulomatosis, aspergilloma, neurofibroma, fungal infection or granuloma (histoplasmosis).

Q: Mention one **investigation** to confirm.

A: CT-guided FNAC.

Q: What **investigations** should be done?

A: As follows:

- CXR lateral view.
- CBC and ESR.
- Sputum for Gm staining, C/S, AFB, malignant cell.
- Mantoux test (MT).
- CT-guided FNAC.
- Bronchoscopy and bronchial brushing for AFB, malignant cell.

Q: How to **differentiate** neurofibroma from dermoid cyst radiologically?

A: By lateral film:

- If neurofibroma: It is in the posterior mediastinum
- If dermoid cyst: It is in the anterior mediastinum.

Multiple Secondaries in Lung



Fig. A: Multiple secondaries in both lungs

Q: Write down the radiological **finding** of the X-ray shown in Figure A.

A: X-ray chest PA view showing multiple, nodular shadows of variable size and shape, some having 'cannon-ball' appearance in both lung fields.

Q: What is your radiological **diagnosis**?

A: Multiple secondary deposits in the lung.

Q: Mention five **sources** of such lesion.

A: As follows:

- Carcinoma stomach.
- Carcinoma of prostate.
- Carcinoma of breast.
- Teratoma.
- Renal cell carcinoma.
- Carcinoma of thyroid gland.



Fig. B: Multiple secondaries in both lungs

Q: Write down the radiological **finding** of the X-ray shown in Figure B.

A: X-ray of chest PA view showing:

- Multiple, nodular shadows of variable size and shape, some having 'cannon-ball' appearance in both lung fields.
- Right dome of diaphragm is elevated.

Q: What is your radiological **diagnosis**?

A: Multiple secondary deposits in the lung with right phrenic nerve palsy.

Consolidation



Right-sided consolidation

Q: Write down the radiological **finding** of this X-ray.

A: X-ray chest PA view showing dense, homogeneous opacity involving the right upper and part of mid zone with air bronchogram within it.

Q: What are the differential **diagnoses** from this X-ray?

A: As follows:

- Consolidation.
- Bronchial carcinoma.
- Tuberculosis.

Q: What is the **likely diagnosis**?

A: Consolidation.

Q: Write down the **percussion and auscultation findings** of this patient.

A: As follows:

- Percussion note is dull (or woody dull).
- Auscultation: Bronchial breath sound, increased vocal resonance.

Q: Write down other **investigations** to confirm the diagnosis.

A: As follows:

- CBC with ESR.
- Sputum for Gram staining, culture and sensitivity.
- Sputum for AFB and malignant cell.

Q: Mention two **complications**?

A: As follows:

- Lung abscess.
- Empyema.

Q: What is the commonest **organism**?

A: Pneumococcus.

Lung Abscess

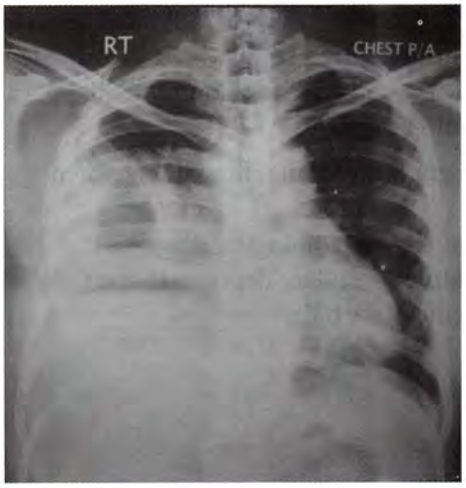


Fig. A: Right-sided lung abscess

Q: Write down the radiological **finding** of the X-ray shown in Figure A.

A: X-ray chest PA view showing a cavity with air–fluid level in the right mid and lower zone.

Q: What is your **diagnosis**?

A: Right-sided lung abscess.

Q: Write down the **percussion and auscultation findings** of this patient.

A: As follows:

- Percussion note is dull (may be dull in the lower part and hyperresonant in the upper part).
- Auscultation: Bronchial breath sound, increased vocal resonance.

Q: What other **investigations** will you do to confirm this diagnosis?

A: As follows:

- CBC with ESR.
- CT scan of chest.
- Sputum for Gram staining, CS and AFB.

Q: Write down three important **complications**.

A: As follows:

- Empyema thoracis.
- Bronchiectasis.
- Cerebral abscess.

Q: What is the commonest **cause**?

A: Aspiration of infected material due to any cause.

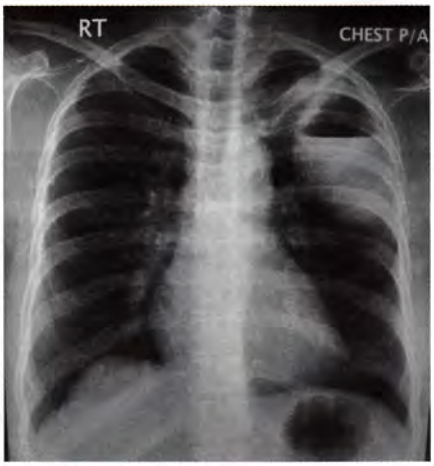


Fig. B: Left-sided lung abscess

Q: Write down the radiological **finding** of the X-ray shown in Figure B.

A: X-ray chest PA view showing a cavity with air–fluid level in the left upper and part of midzone.

Q: What is your **diagnosis**?

A: Left-sided lung abscess.

Pulmonary Tuberculosis



Fig. A: Right-sided pulmonary tuberculosis

Q: Write down the radiological **finding** of the X-ray shown in Figure A.

A: X-ray chest PA view showing patchy opacities with some translucent shadows within it involving right upper and part of mid-zone.

Q: What is the radiological **diagnosis**?

A: Right-sided pulmonary tuberculosis.

Q: Write down other **investigations** to confirm the diagnosis.

A: As follows:

- CBC with ESR.
- Sputum for AFB staining (three consecutive samples).
- Tuberculin test.
- PCR for TB.

Q: How to **treat**?

A: Standard anti-TB therapy for 6 months in the following regimen:

- Initial phase (2 months): Isoniazid (INH) + Rifampicin + Pyrazinamide + Ethambutol.
- Continuation phase (4 months): INH + Rifampicin.
- Tab. Pyridoxine (20 mg) for 6 months.

Q: Mention one **complication** of each drug.

A: As follows:

- Rifampicin: Hepatitis.
- INH: Peripheral neuropathy.
- Ethambutol: Optic neuritis.
- Pyrazinamide: Hepatitis (also hyperuricaemia and gout).



Fig. B: Bilateral extensive tuberculosis

Q: Write down the radiological **finding** of the X-ray shown in Figure B.

A: X-ray chest PA view showing patchy opacities involving both upper and middle zone in both right and left lung.

Q: What is the radiological **diagnosis**?

A: Bilateral extensive tuberculosis.



Fig. C: Tubercular cavity in left side

Q: Write down the radiological **finding** of the X-ray shown in Figure C.

A: X-ray chest PA view showing patchy opacities with cavity in the left upper zone.

Q: What is the radiological **diagnosis**?

A: Pulmonary tuberculosis.

Q: What is the **significance** of this finding?

A: Presence of cavity indicates active and open case of tuberculosis.

Miliary Tuberculosis



Miliary tuberculosis

Q: Write down the radiological **finding** of this X-ray.

A: X-ray chest PA view showing multiple miliary mottling involving all the zones of both lung fields.

Q: What is the **diagnosis**?

A: Miliary tuberculosis.

Q: Mention four common **differential** diagnoses.

A: As follows:

- Sarcoidosis.
- Pulmonary eosinophilia.
- Histoplasmosis.
- Pneumoconiosis.

Q: Mention four **investigations**.

A: As follows:

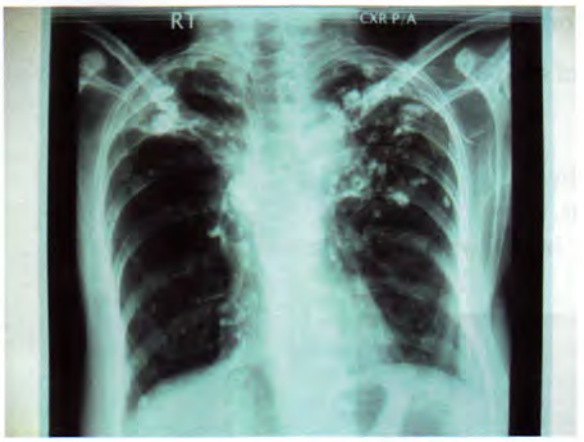
- CBC with ESR and circulating eosinophil count.

- Sputum for AFB.
- Tuberculin test.
- Bronchoscopy and bronchoalveolar lavage.

Q: What are the common **presentations** of this patient?

A: Low-grade continued fever, mostly evening rise, night sweat, weight loss, cough with haemoptysis, etc.

Calcification of the Lung Parenchyma



Calcification of lung parenchyma

Q: Write down the radiological **findings** in this X-ray.

A: X-ray chest PA view showing multiple calcified shadows of variable size and shape, involving all the zones of both lung fields.

Q: What is your radiological **diagnosis**?

A: Multiple calcifications in lung parenchyma.

Q: Mention five **causes**.

A: As follows:

- Tuberculosis (usually healed, commonly in upper zone).
- Adult chicken pox pneumonia (widely distributed, usually small, 1–3 mm).
- Histoplasmosis (surrounded by small halo) and other fungal infection.
- Hamartoma (popcorn calcification).
- Hypercalcaemia due to any cause.
- Alveolar microlithiasis.
- Silicosis.

Emphysema



Emphysema

Q: Write down the radiological **finding** of this X-ray.

A: CXR PA view showing:

- Lung fields are hypertranslucent.
- Low and flat diaphragm.
- Heart is elongated and tubular.
- Ribs are widely spaced.

Q: What is your radiological **diagnosis**?

A: Pulmonary emphysema.

Q: What is the **pathognomonic sign** in CXR of this disease?

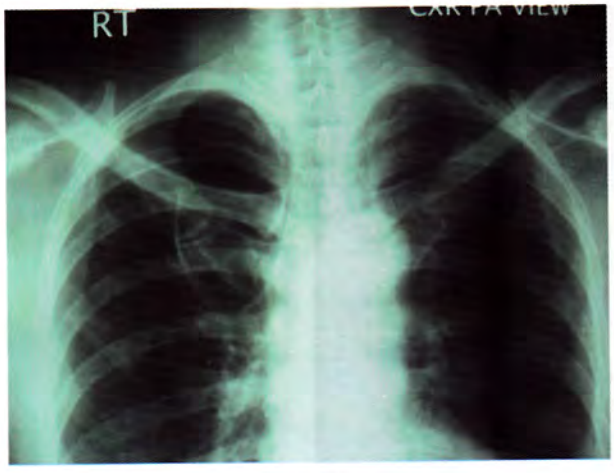
A: Bullae.

Q: Mention two **investigations**.

A: As follows:

- Lung function tests (obstructive type: FEV_1 and FVC are reduced and ratio of FEV_1:FVC is also reduced).
- High resolution computed tomography (HRCT) of chest.

Bullae



Bullae

Q: Write down the radiological **findings** in this X-ray.
A: X-ray chest PA view showing a large translucent area in the right upper zone with no lung marking and blood vessel, bounded by a thin-line (hairline) shadow.

Q: What is your radiological **diagnosis**?
A: Right-sided giant bullae.

Q: What are the **other possibilities**?
A: As follows:

- Apical pneumothorax (collapsed lung margin should be present in such case).
- Big cavity.

Q: Mention three **complications**.
A: As follows:

- Rupture causing pneumothorax.
- Secondary infection.
- Aspergilloma.

Surgical Emphysema



Surgical emphysema with bilateral chest tube

Q: Write down the radiological **findings** in this X-ray.
A: X-ray chest PA view showing:

- Increased translucency with collapsed lung margin on the right side.
- There are multiple translucent shadows in the soft tissue outside the thoracic cavity in both sides.
- Intrathoracic tube (IT tube) is seen on both sides.

Q: What is your radiological **diagnosis**?
A: Right-sided pneumothorax with subcutaneous emphysema.

Q: Mention three **causes**.
A: As follows:

- Traumatic (road traffic accident, penetrating injury).
- During aspiration of pneumothorax or introduction of IT tube.
- Acute severe asthma (due to rupture of alveoli).
- Intermittent positive pressure ventilation.

Pneumothorax

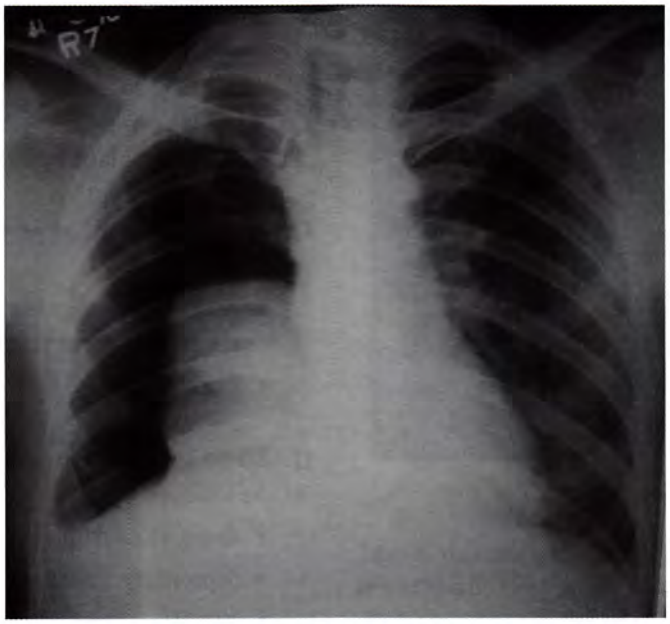


Fig. A: Right-sided pneumothorax

Q: Write down the radiological **findings** of the X-ray shown in Figure A.

A: X-ray chest PA view showing hypertranslucent area without bronchovascular markings with collapsed lung margin in right side.

Q: What is the radiological **diagnosis**?

A: Right-sided pneumothorax.

Q: What is the **type**?

A: Closed.

Q: Write down the **findings** in percussion and auscultation.

A: As follows:

- Percussion note is hyperresonant on left side.
- On auscultation: Diminished (or absent) breath sound and diminished (or absent) vocal resonance on left side.

Q: Write down three common **causes**.

A: As follows:

- Rupture of subpleural emphysematous bullae.
- Rupture of subpleural tuberculous focus.
- Rupture of subpleural bleb in young patient.

Q: Write down the **principle of management** of this patient.

A: As follows:

- If small and asymptomatic: Complete rest and follow-up.
- If large: Intercostal chest tube drainage (or water seal drainage).
- Treatment of underlying cause.



Fig. B: Left-sided pneumothorax

Q: Write down the radiological **findings** of the X-ray shown in Figure B.

A: X-ray chest PA view showing hypertranslucent area without bronchovascular markings with collapsed lung margin in left side.

Q: What is the radiological **diagnosis**?

A: Left-sided pneumothorax.

Hydropneumothorax



Right-sided hydropneumothorax

Q: Write down the radiological **findings** of this X-ray.
A: X-ray chest PA view showing:

- Increased translucency with collapse lung margin on the right side.
- There is a horizontal fluid level with obliteration of right costophrenic and cardiophrenic angles.

Q: What is your radiological **diagnosis**?
A: Right-sided hydropneumothorax.

Q: Mention one **important bedside physical finding**.
A: Succussion splash.

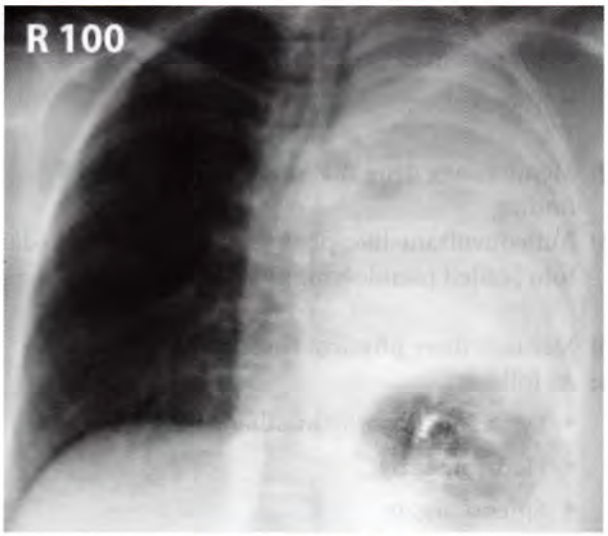
Q: What are the **causes**?
A: As follows:

- Iatrogenic (during aspiration of pleural fluid)—common cause.
- Bronchopleural fistula.
- Trauma (penetrating injury, thoracic surgery).
- Rupture of lung abscess.
- Oesophageal rupture.
- Erosion by bronchial carcinoma.
- Pulmonary tuberculosis.

Q: How to **treat**?
A: As follows:

- Insertion of intrathoracic tube.
- Treatment of specific cause.

Collapse of Lung



Collapse of left lung

Q: What is your radiological **finding**?
A: X-ray chest PA view showing:

- Homogenous opacity involving the whole left lung field.
- Trachea and heart shifted to the left.
- Hypertranslucency of the right lung field.

Q: What is your radiological **diagnosis**?
A: Collapse of the left lung.

Q: Mention two **causes**.
A: As follows:

- Bronchial carcinoma with complete bronchial obstruction.
- Foreign body in the left bronchus.

Q: Mention three **physical findings**.
A: As follows:

- Palpation: Trachea and apex beat shifted to the left.
- Percussion: Dullness in the whole left hemithorax.
- Auscultation: Breath sound and vocal resonance are diminished in the left side.

Q: Mention two further **investigations**.
A: As follows:

- CT scan of the chest.
- Bronchoscopy.

Rib Resection



Rib resection

Q: Write down the radiological **findings** in this X-ray.
A: X-ray chest PA view showing:

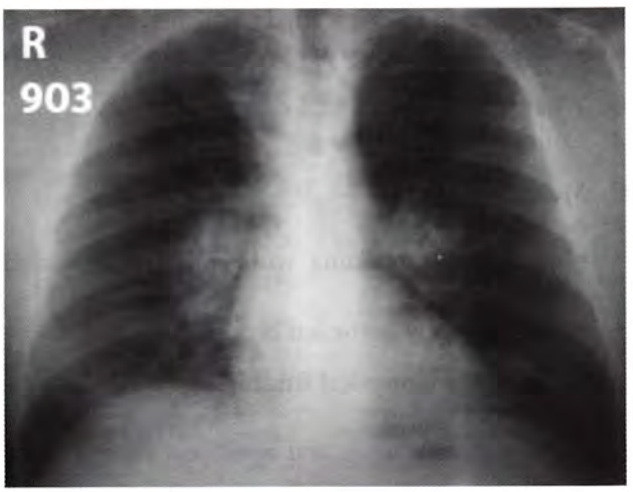
- There is rib resection on the left side.
- Homogeneous opacity with air-fluid level involving the left lower and part of middle zone. The rest of the left lung field shows hypertranslucency.
- Left costophrenic and cardiophrenic angles are obscure.
- Trachea and heart are shifted to the left.
- The right lung field shows compensatory hypertranslucency.

Q: What is your radiological **diagnosis**?
A: Pneumonectomy of left lung.

Q: Mention five **indications**.
A: As follows:

- Bronchial carcinoma (if localized).
- Bronchial adenoma.
- Extensive bronchiectasis.
- Extensive fibrosis with repeated chest infection.
- In some cases of TB [multidrug-resistant TB (MDR-TB) or no response to drug].

Bilateral Hilar Lymphadenopathy



Bilateral hilar lymphadenopathy

Q: Write down the radiological **finding** of this X-ray.
A: X-ray chest PA view showing bilateral hilar lymphadenopathy.

Q: Write three **causes**.
A: As follows:

- Sarcoidosis.
- Lymphoma.
- Tuberculosis.

Q: Mention one **drug** that can cause this type of finding.
A: Anticonvulsant like phenytoin or diphenylhydantoin (called pseudolymphoma).

Q: Mention three **physical findings**.
A: As follows:

- Lymphadenopathy in other parts of the body.
- Hepatomegaly.
- Splenomegaly.

Q: Write two **investigations**.
A: As follows:

- CBC, ESR.
- Tuberculin test.
- FNAC or biopsy from lymphnode.

Sarcoidosis



Bilateral hilar lymphadenopathy with parenchymal lung involvement

Q: Write down the radiological **finding** of this X-ray.

A: X-ray chest PA view showing:

- Bilateral hilar lymphadenopathy.
- Reticulonodular shadow in both lung fields.

Q: What is your radiological **diagnosis**?

A: Sarcoidosis.

Q: Mention four **physical findings**.

A: As follows:

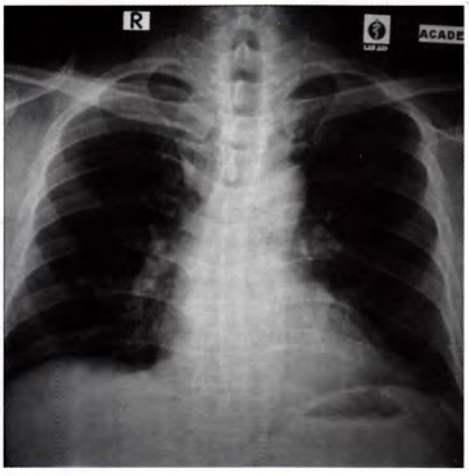
- Erythema nodosum.
- Lymphadenopathy in other parts of the body.
- Hepatosplenomegaly.
- Bilateral parotid enlargement.

Q: Write three **investigations** to confirm.

A: As follows:

- Tuberculin test (usually 0).
- FNAC or biopsy from the lymphnode.
- Bronchoscopy and biopsy.

Azygos Lobe



Azygos lobe

Q: Write down the radiological **finding** of this X-ray.

A: X-ray chest PA view showing an inverted-comma-shaped opacity in the right apical region.

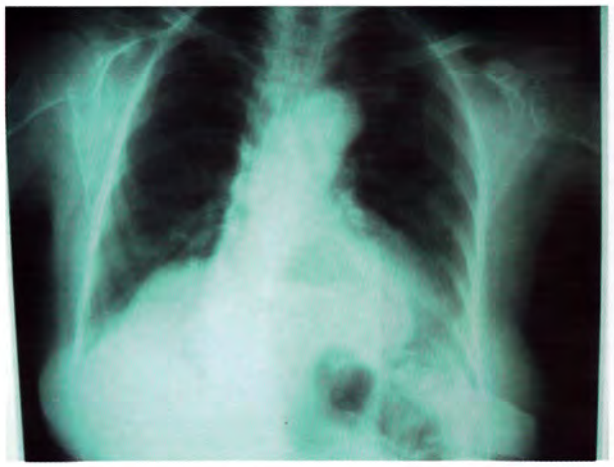
Q: What is your radiological **diagnosis**?

A: Azygos lobe.

Q: What is the **significance**?

A: It is physiological and may be confused with pathological conditions such as consolidation, TB and mass lesion.

Cavity Superimposed on Cardiac Shadow



Cavity superimposed on cardiac shadow

Q: Write down the radiological **finding** of this X-ray.

A: X-ray chest PA view showing air–fluid level superimposed on cardiac shadow.

Q: Mention three **differential** diagnoses.

A: As follows:

- Hiatus hernia.
- Achalasia cardia.
- Lung abscess.

Q: Mention three **investigations**.

A: As follows:

- Chest X-ray left lateral view.
- Barium swallow of oesophagus in Trendelenburg position.
- Endoscopy.

Bronchiectasis



Fig. A: Bilateral bronchiectasis

Q: Write down the radiological **findings** of the X-ray shown in Figure A.

A: X-ray chest PA view showing multiple ring shadows involving the mid and lower zones of both lung fields, more on the right side.

Q: What is your radiological **diagnosis**?

A: Bilateral bronchiectasis

Q: What is the **likely cause** in this disease?

A: Cystic fibrosis.

Q: Write down **one investigation** to confirm the diagnosis.

A: HRCT of chest.



Fig. B: Right-sided bronchiectasis

Q: Write down the radiological **findings** of the X-ray shown in Figure B.

A: X-ray chest PA view showing multiple ring shadows involving the lower zone of right lung field.

Q: What is your radiological **diagnosis**?

A: Right-sided bronchiectasis.

Q: What is the **commonest cause**?

A: Childhood pneumonia or pulmonary infection after whooping cough and measles.

Q: What is the **definitive treatment** of this case?

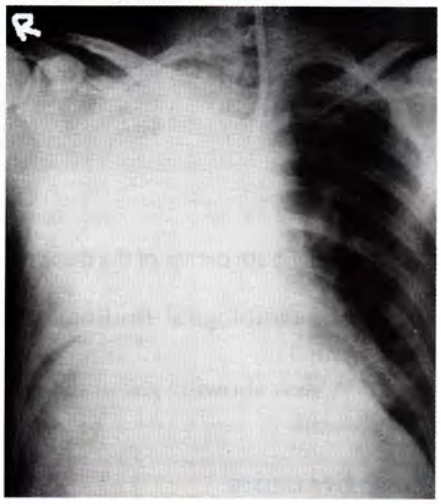
A: Lobectomy.

Q: Mention three other **treatment** modalities.

A: As follows:

- Postural drainage.
- Chest physiotherapy.
- Antibiotic, if infection is present.

Homogeneous Opacity of One Hemithorax



Homogenous opacity of right lung

Q: Write down the radiological **findings** of this X-ray.

A: X-ray chest PA view showing homogenous opacity involving the whole right hemithorax.

Q: Mention three **differential diagnoses**.

A: As follows:

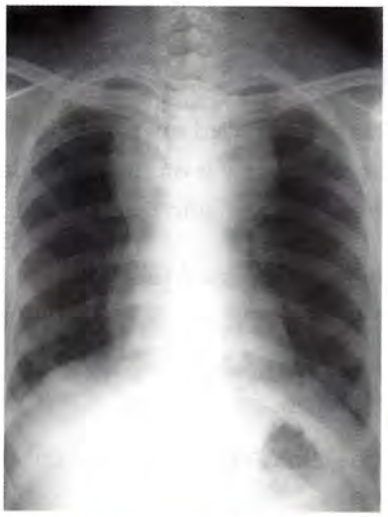
- Massive consolidation.
- Massive pleural effusion.
- Complete collapse of right lung.

Q: Mention three **investigations**.

A: As follows:

- CT scan of chest.
- Bronchoscopy and biopsy.
- CT-guided FNAC.

Mediastinal Widening



Mediastinal widening

Q: Write down the radiological **findings** of this X-ray.

A: X-ray chest PA view showing widening of the superior mediastinum.

Q: Mention four differential **diagnoses**.

A: As follows:

- Lymphoma.
- Sarcoidosis.
- Bronchial carcinoma.
- Retrosternal goitre.

Q: Mention one important **physical finding** of this patient.

A: Puffiness of the face with engorged, nonpulsatile neck veins due to superior vena caval obstruction.

Q: Mention four other **investigations**.

A: As follows:

- CBC.
- X-ray chest lateral view.
- CT scan of chest.
- CT-guided FNAC.

Gas Under the Diaphragm



Fig. A: Gas under the right dome of the diaphragm

Q: Write down the radiological **findings** of the X-ray shown in Figure A.

A: X-ray chest PA view showing gas under the right dome of diaphragm.

Q: What is your radiological **diagnosis**?

A: Perforation of gas containing hollow viscus.

Q: Write down two common **causes**.

A: As follows:

- Perforation of chronic duodenal ulcer.
- Perforation of ileum (due to typhoid, tuberculosis, Crohn disease).

Q: Mention one most important **clinical finding**.

A: Obliteration of liver dullness on percussion.

Q: Write down the modalities of treatment.

A: As follows:

- Nothing by mouth.
- Nasogastric suction.
- Intravenous (IV) fluid.
- Broad spectrum antibiotic with metronidazole.
- Surgical repair.



Fig. B: Gas under both domes of the diaphragm

Q: Write down the radiological **findings** of the X-ray shown in Figure B.

A: X-ray chest PA view showing gas under both domes of the diaphragm.

Q: Write down five **causes**.

A: As follows:

- Perforation of hollow viscus containing gas.
- Laparotomy or laparoscopy.
- Penetrating injury of abdomen.
- Burst appendicitis.
- Tubal insufflation.

Situs Inversus



Situs inversus

Q: Write down the radiological **finding** of this X-ray.

A: X-ray chest PA view showing:

- Cardiac apex directed towards right side.
- Fundic gas shadow is on the right side.
- Left dome of the diaphragm is raised.

Q: What is your radiological **diagnosis**?

A: Situs inversus.

Q: What is the **prognosis**?

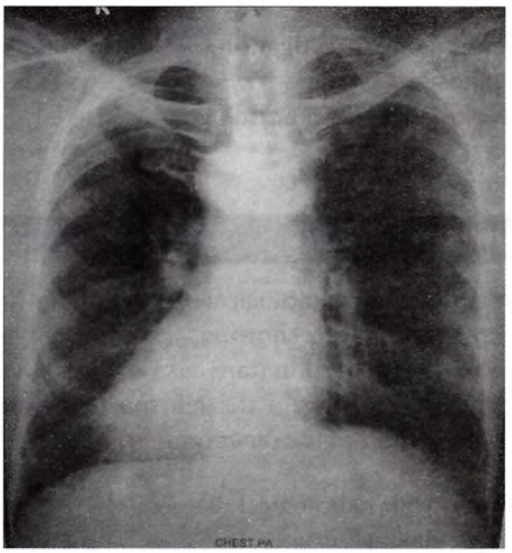
A: Normal lifespan.

Q: What is the clinical **importance** of this disorder?

A: As follows:

- Patient's appendix is on the left side. So, the appendicitis may be missed as it is on the left side.
- Sometimes, liver biopsy is done mistakenly on the right side; it will be missed.

Dextrocardia



Dextrocardia

Q: Write down the radiological **finding** of this X-ray.

A: X-ray chest PA view showing:

- Cardiac apex directed towards right side.
- Fundic gas shadow is on the left side.

Q: What is your radiological **diagnosis**?

A: Dextrocardia.

Q: What other **investigation** should be done? Why?

A: X-ray of paranasal sinuses (PNS) to see sinusitis or frontal sinus agenesis, which may be present in Kartagener syndrome.

N.B. Kartagener syndrome is characterized by dextrocardia, bronchiectasis and frontal sinus agenesis or sinusitis.

Mitral Stenosis



Fig. A: Mitral stenosis

Q: Write down the radiological **finding** of the X-ray shown in Figure A.

A: X-ray chest PA view showing fullness of the pulmonary conus with straightening of the left border of the heart.

Q: What is your radiological **diagnosis**?

A: Mitral stenosis.

Q: Mention four important radiological **findings that may be present** in this disease.

A: As follows:

- Widening of the carina with horizontal left main bronchus.
- Double contour of the right heart border.
- Upper lobe diversion.
- Kerley B line.

Q: Mention one **investigation** to confirm your diagnosis.

A: Colour Doppler echocardiography.

Q: Mention two **complications**.

A: As follows:

- Congestive cardiac failure (CCF).
- Atrial fibrillation.



Fig. B: Mitral stenosis with mitral regurgitation

Q: Write down the radiological **finding** of the X-ray shown in Figure B.

A: X-ray chest PA view showing:

- Straightening of the left cardiac border.
- Heart is enlarged in transverse diameter.

Q: What is your radiological **diagnosis**?

A: Mitral stenosis with mitral regurgitation.

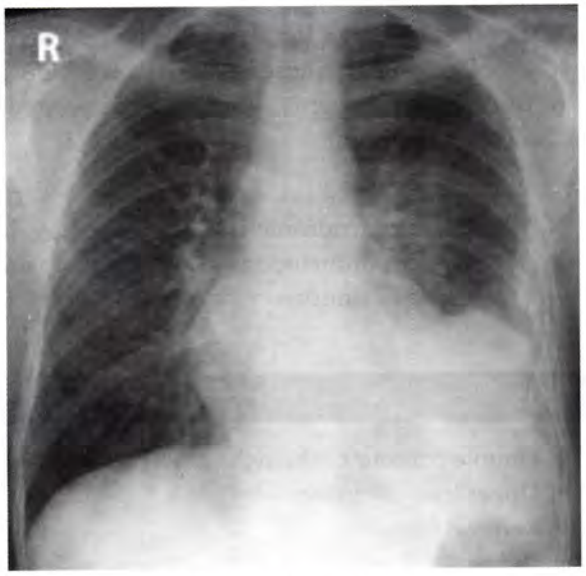
Q: What is the **predominant** lesion?

A: Mitral regurgitation (as heart is enlarged).

Q: Mention one **investigation** to confirm your diagnosis.

A: Colour Doppler echocardiography.

Ventricular Aneurysm



Ventricular aneurysm

Q: Write down the radiological **finding** of this X-ray.

A: X-ray chest PA view showing:

- Heart is enlarged in transverse diameter.
- There is bulging of the left lower border with calcification of the outer border.

Q: What is your radiological **diagnosis**?

A: Ventricular aneurysm.

Q: Mention one investigation to **confirm** your diagnosis.

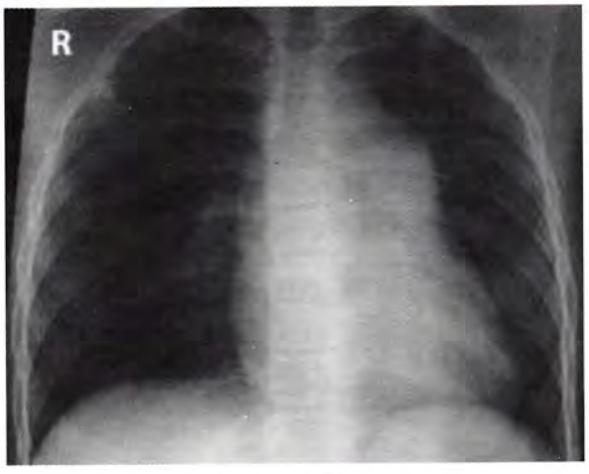
A: Echocardiography.

Q: Mention three **complications**.

A: As follows:

- Acute left ventricular failure (LVF).
- Arrhythmia.
- Systemic embolism.

Atrial Septal Defect



Atrial septal defect

Q: Write down the radiological **finding** of this X-ray.

A: X-ray chest PA view showing:

- Heart is enlarged in transverse diameter.
- There is fullness of the pulmonary conus with bulging of the left border.

Q: What is your radiological **diagnosis**?

A: Atrial septal defect.

Q: Mention one investigation to **confirm** your diagnosis.

A: Colour Doppler echocardiography.

Q: Mention three **auscultatory findings**.

A: As follows:

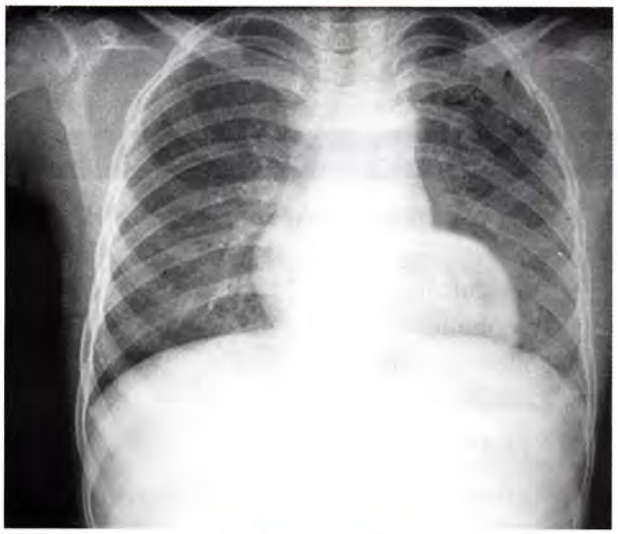
- Wide, fixed splitting of second heart sound.
- Mid-diastolic murmur.
- Ejection systolic murmur.

Q: Mention the **ECG finding**.

A: As follows:

- In ostium primum defect: Right bundle-branch block (RBBB) with left-axis deviation.
- In ostium secundum defect: RBBB with right-axis deviation.

Tetralogy of Fallot



Tetralogy of Fallot

Q: Write down the radiological **finding** of this X-ray.
A: CXR PA view showing:
- Boot-shaped heart (apex is lifted up and there is concavity or bay in the region of pulmonary artery).
- Oligaemic lung fields.

Q: What is your radiological **diagnosis**?
A: Tetralogy of Fallot (TOF).

Q: Mention the **anatomical defects** in this disease.
A: As follows:
- Pulmonary stenosis (valvular or infundibular).
- Overriding and dextroposition of aorta (aortic origin two-third from the left ventricle and one-third from the right ventricle).
- Right ventricular hypertrophy.
- Ventricular septal defect (VSD) (large subaortic).

Q: What are the **physical findings**?
A: As follows:
- Clubbing and central cyanosis.
- Palpation: Left parasternal lift, epigastric pulsation and systolic thrill in pulmonary area.
- Auscultation: First heart sound is normal, P2 is soft or absent in pulmonary area, A2 is normal. Harsh ejection systolic murmur in pulmonary area radiating to suprasternal notch.

Q: What are the **complications**?
A: As follows:
- Infective endocarditis.
- Paradoxical emboli.
- Cerebral abscess (in 10% cases).
- Polycythaemia secondary to hypoxia (it may cause cerebral infarction).

Q: Mention two **investigations**.
A: As follows:
- Colour Doppler echocardiogram.
- Cardiac catheter.

Q: How to **treat**?
A: As follows:
- Surgical correction should be done.
- If total correction is not possible, then temporarily Blalock–Taussig shunt is performed. Corrective surgery is done later on.
- Prophylactic antibiotic to prevent infective endocarditis.

Cardiomegaly



Cardiomegaly

Q: Write down the radiological **finding** of this X-ray.
A: X-ray chest PA view showing increased transverse diameter of cardiac shadow.

Q: What is the radiological **diagnosis**?
A: Cardiomegaly.

Q: Mention five important common **causes** of producing this X-ray finding.
A: As follows:
- Pericardial effusion.
- Multiple valvular heart disease.
- Biventricular failure.
- Myocarditis.
- Cardiomyopathy.

- Shunt anomaly (VSD, ASD, PDA).
- Hyperdynamic circulation due to any cause (anaemia, beriberi, thyrotoxicosis, arteriovenous fistula, etc.).

Q: What other **investigations** should be done?

A: As follows:

- ECG.
- Echocardiogram.

Pericardial Effusion



Pericardial effusion

Q: Write down the radiological **findings** of this X-ray.

A: X-ray chest PA view showing:

- Heart is enlarged in transverse diameter, globular, pear shaped with clear margin.
- Lung fields are oligaemic.

Q: What is the radiological **diagnosis**?

A: Pericardial effusion.

Q: Name five common **causes** of pericardial effusion.

A: As follows:

- Tuberculosis.
- Lymphoma.
- Following acute pericarditis.
- Collagen diseases.
- Myxoedema.

Q: Write down four important **signs** in favour of your diagnosis.

A: As follows:

- Raised jugular venous pressure (JVP).
- Narrow pulse pressure, may be pulsus paradoxus.
- Heart sounds are muffled or absent.
- Enlarged, tender liver.

Q: Name one **investigation** to confirm the diagnosis.

A: Echocardiogram.

Q: Mention one **serious complication** of this. How to manage?

A: Cardiac tamponade. Managed by immediate paracentesis.

Pericardial Calcification

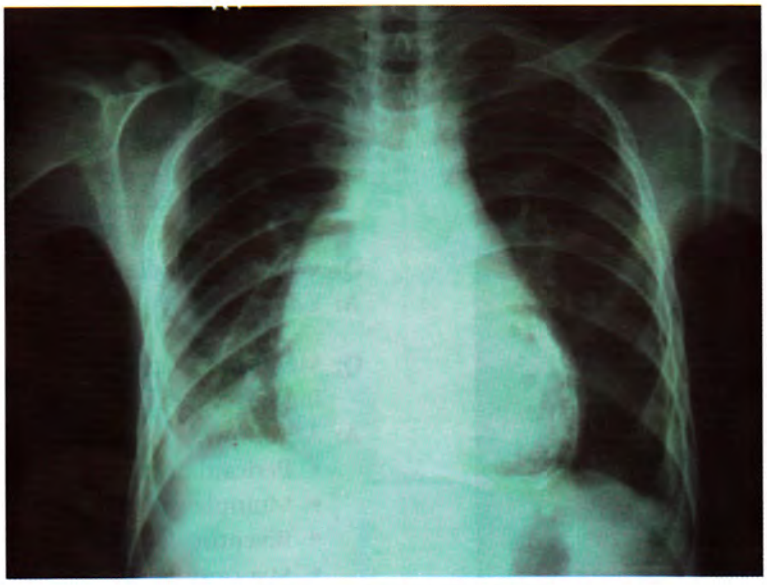


Fig. A: Pericardial calcification

Q: Write down the radiological **finding** of the X-ray shown in Figure A.

A: X-ray chest PA view showing:

- Calcified shadow at the left and lower border of heart.
- Heart is enlarged in transverse diameter.

Q: What is your radiological **diagnosis**?

A: Pericardial calcification.

Q: What is the **clinical diagnosis**?

A: Chronic constrictive pericarditis.

Q: Mention three **causes**.

A: As follows:

- Tuberculosis.
- Hypercalcaemia due to any cause.
- Haemopericardium.

Q: Write down the radiological **finding** of the X-ray shown in Figure B.

A: X-ray chest left lateral view showing flecks of calcification in the pericardium at inferior and anterior border.

Q: What is your radiological **diagnosis**?

A: Pericardial calcification.

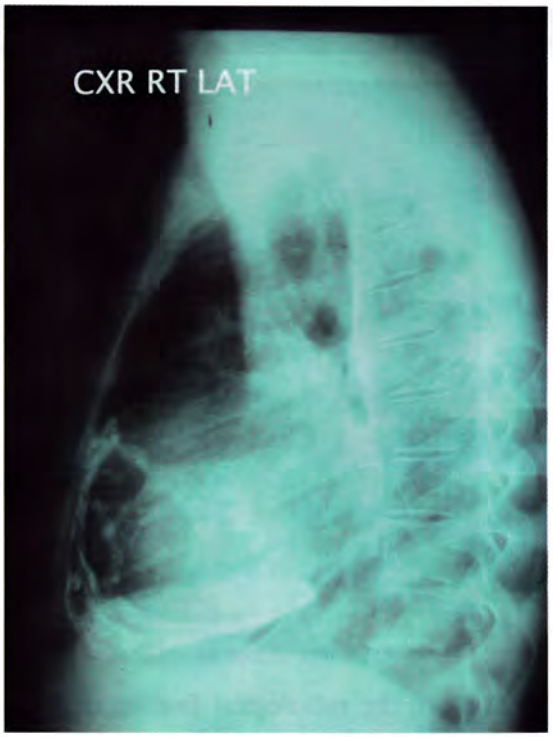
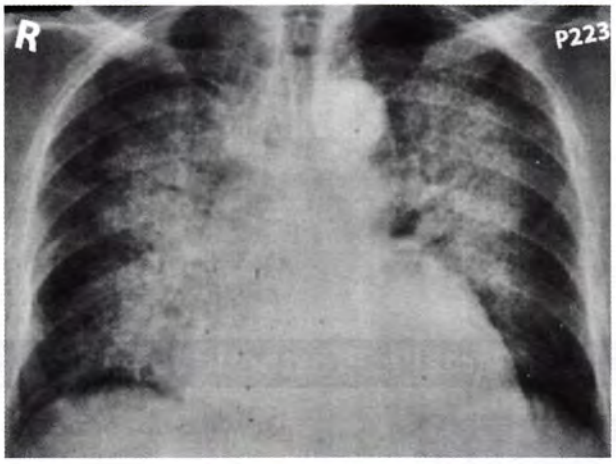


Fig. B: Pericardial calcification (lateral view)

Pulmonary Oedema



Pulmonary oedema

Q: Write down the radiological **finding** of this X-ray.

A: CXR PA view showing:

- Fluffy or woolly opacities, spreading from both hilar-region, giving a butterfly- or bat's-wing appearance.
- Heart is enlarged in transverse diameter.

Q: What is your radiological **diagnosis**?

A: Pulmonary oedema.

Q: Mention three **causes**.

A: As follows:

- Acute LVF due to any cause.
- Mitral stenosis.
- Excessive or rapid transfusion of fluid or blood.

Q: How to **manage**?

A: As follows:

- Propped-up position.
- Oxygen inhalation 4–6 L/min (60–100%).
- Injection frusemide IV.
- Injection morphine 10–20 mg IV, with cyclizine or metoclopramide if vomiting.
- Angiotensin-converting-enzyme (ACE) inhibitor (captopril, lisinopril), vasodilator (isosorbide) and digoxin (in some cases).
- Treatment of primary cause.

Pacemaker

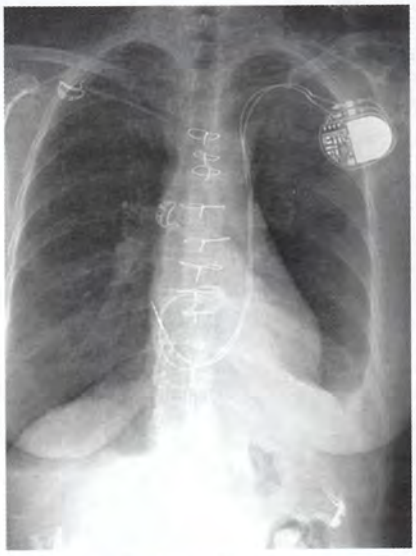


Fig. A: Dual-chamber pacemaker

Q: Write down the radiological **finding** of the X-ray shown in Figure A.

A: X-ray chest PA view showing:

- Metallic suture wire of sternotomy.
- Dual-chamber pacemaker on the left side.

Q: What is your radiological **diagnosis**?

A: Dual-chamber pacemaker.

Q: Mention two common **indications**.

A: As follows:

- Complete heart block (with syncope or Stokes–Adams attack).
- Sick sinus syndrome.

Q: Mention five **complications**.

A: As follows:

- Infection.
- Displacement.
- Malfunction or pacemaker failure.
- Pacemaker-mediated tachycardia (by dual-chamber pacing).
- Pacemaker syndrome (occurs in single-chamber pacing).

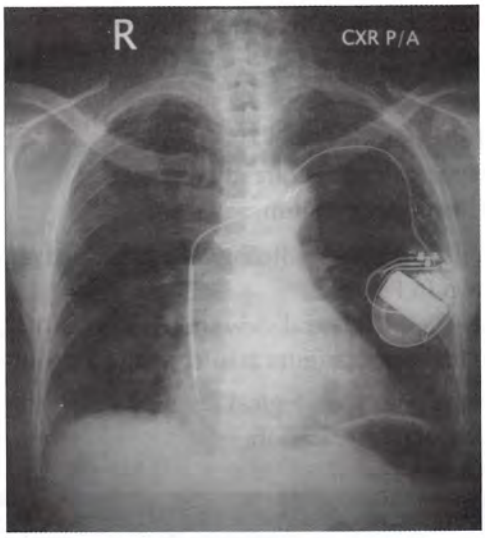


Fig. B: Single-chamber pacemaker

Q: Write down the radiological **finding** of the X-ray shown in Figure B.

A: X-ray chest PA view showing:

- Metallic suture wire of sternotomy.
- Single-chamber pacemaker on the left side.

Q: What is your radiological **diagnosis**?

A: Single-chamber pacemaker.

Metallic Prosthetic Valve



Fig. A: Metallic prosthetic mitral valve

Q: Write down the radiological **finding** of the X-ray shown in Figure A.

A: X-ray chest PA view showing:

- Metallic wire of suture in the sternum (indicates sternotomy).
- A metallic prosthetic heart valve.

Q: What is your **radiological** diagnosis?

A: Metallic prosthetic mitral valve.

Q: Mention two **complications**.

A: As follows:

- Infective endocarditis.
- Valve failure.

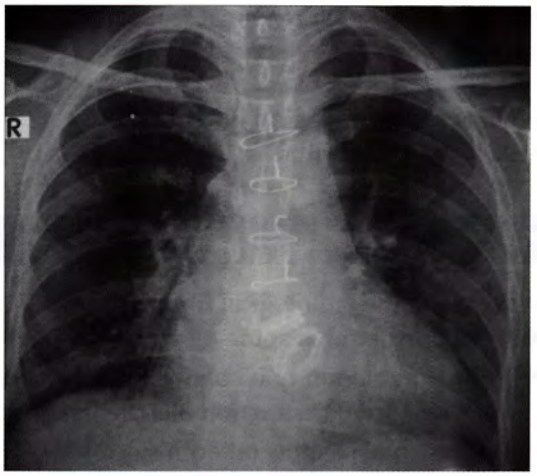


Fig. B: Metallic prosthetic mitral and aortic valve

Q: Write down the radiological **finding** of the X-ray shown in Figure B.

A: X-ray chest PA view showing:

- Metallic wire of suture in the sternum (indicates sternotomy).
- Two metallic prosthetic heart valves.

Q: What is your **radiological** diagnosis?

A: Metallic prosthetic mitral and aortic valves.

Ankylosing Spondylitis



Fig. A: Ankylosing spondylitis

Q: What are your **findings** in the X-ray shown in Figure A?

A: X-ray of lumbosacral spine anteroposterior (AP) view showing:

- Calcification of anterior longitudinal and interspinous ligaments.
- There is syndesmophyte formation with bridging, giving rise to bamboo-spine appearance.

Q: What is your radiological **diagnosis**?

A: Ankylosing spondylitis.

Q: Mention one **bedside test.**

A: Schober test.

Q: Write one **investigation** that is helpful for your diagnosis.

A: HLA-B27.



Fig. B: Ankylosing spondylitis

Q: What are your **findings** in the X-ray shown in Figure B?

A: X-ray of lumbosacral spine lateral view showing:

- Syndesmophyte formation along the corners of vertebral body with bridging, giving rise to bamboo-spine appearance.
- Osteopaenia with marginal sclerosis of vertebral body.

Q: What is your radiological **diagnosis**?

A: Ankylosing spondylitis.

Pott Disease



Pott disease

Q: Write down the radiological **finding** of this X-ray.

A: X-ray of dorsolumbar spine AP view showing:

- Reduction of joint space between T6, T7 and also T8, with partial destruction of vertebral body.
- Paravertebral shadow on both sides.
- There is marginal sclerosis.

Q: What is your radiological **diagnosis**?

A: Pott disease (tuberculosis of spine or tuberculous spondylitis).

Q: Mention three **investigations**.

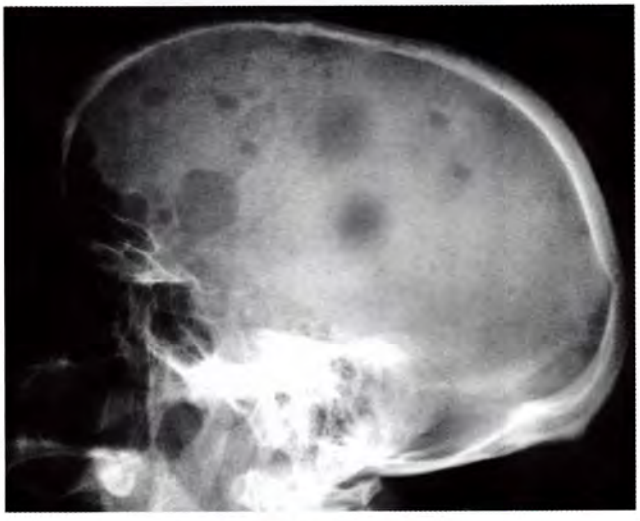
A: As follows:

- CBC, ESR.
- X-ray chest PA view (to see primary focus).
- Tuberculin test.
- MRI of thoracic spine.

Q: How to **confirm**?

A: CT or ultrasonogram-guided FNAC.

Multiple Myeloma



Multiple myeloma

Q: Write down the radiological **finding** of this X-ray.

A: X-ray of skull in lateral view showing multiple punched-out lytic lesions of variable sizes and shapes all over the skull.

Q: What is the most likely **diagnosis**?

A: Multiple myeloma.

Q: Write two important **differential** diagnoses.

A: As follows:

- Secondary deposit.
- Hyperparathyroidism.

Q: Name other investigations to **confirm** the diagnosis.

A: As follows:

- CBC with ESR with peripheral blood film (PBF) (shows high ESR with marked rouleaux formation).
- Bone marrow examination (shows atypical plasma cells).
- Plasma protein electrophoresis (shows M-band).
- Serum immunoelectrophoresis.
- Urine for Bence–Jones protein.

Hereditary Haemolytic Anaemia



Fig. A: Thalassaemia

Q: Write down the radiological **finding** of the X-ray shown in Figure A.

A: X-ray of skull in lateral view showing:

- Widening of diploic space.
- Thinning of outer table.
- Thickening and coarsening of trabeculae, giving rise to hair-on-end appearance.

Q: What is the most likely **diagnosis**?

A: Hereditary haemolytic anaemia, most likely β-thalassaemia major.

Q: Name four **examples**.

A: As follows:

- β-Thalassaemia major.
- Haemoglobin E disease (more common).
- Thalassaemia E disease (double heterozygous).
- Hereditary spherocytosis.

Q: Write down five important **physical findings** in this patient.

A: As follows:

- Anaemia.
- Jaundice.
- Splenomegaly.
- Frontal and parietal bossing.
- Mongoloid facies.

Q: Mention one **investigation** to confirm the diagnosis.

A: Haemoglobin electrophoresis.

Q: Mention one **simple investigation** helpful for the diagnosis.

A: CBC with PBF (microcytic hypochromic anaemia).

Q: What **investigations** should be done in this patient?

A: As follows:

- CBC with PBF (microcytic hypochromic anaemia).
- Reticulocyte count by supravital stain (usually high in haemolytic anaemia).
- Serum bilirubin (increased).
- Haemoglobin electrophoresis (shows absent or grossly reduced HbA and increased HbF in β-thalassaemia major. In case of β-thalassaemia minor, HbA2 is increased).



Fig. B: X-ray of hands in hereditary haemolytic anaemia

Q: Write down the radiological **finding** of the X-ray shown in Figure B.

A: X-ray of both hands in anteroposterior view showing:

- Widening of medullary cavity.
- Thinning of cortex.
- Reduction of number of trabeculae and thickening of remaining trabeculae.
- Generalized osteopaenia.

Q: What is the most likely **diagnosis**?

A: Hereditary haemolytic anaemia.

Acromegaly



Acromegaly

Q: What are your radiological **findings**?
A: X-ray of skull in lateral view showing:
- Skull is enlarged.
- Frontal sinus is enlarged.
- Sella turcica is enlarged.
- There is erosion of anterior and posterior clinoid process.

Q: What is your radiological **diagnosis**?
A: Acromegaly (due to pituitary adenoma).

Q: What other **investigations** should be done.
A: As follows:
- X-ray of hands and feet (to see heel pad).
- Magnetic resonance imaging (MRI) of skull.
- Growth hormone (GH) assay (radioimmunoassay).
- Glucose tolerance test with simultaneous measurement of GH.
- Measurement of insulin-like growth factor-1 (IGF-1) (also called somatomedin C).
- Assessment of other anterior pituitary hormones.
- Perimetry (bitemporal hemianopia).

Q: Mention one specific **treatment**.
A: Trans-sphenoidal removal of adenoma.

Q: Mention two **drugs** that can be used.
A: As follows:
- Somatostatin analogue, e.g. octreotide or lanreotide.
- Bromocriptine (dopamine agonist).
- Pegvisomant (a peptide GH receptor antagonist).

Tophi



Tophi

Q: What are your radiological **findings**?
A: X-ray of left foot showing:
- Two bony outgrowths—one large involving the first MTP joint and one small in the second distal interphalangeal (DIP) joint.
- Presence of lytic lesion.
- Destruction of the first interphalangeal joint.

Q: What is your radiological **diagnosis**?
A: Chronic tophaceous gout.

Q: How to **confirm** your diagnosis?
A: As follows:
- Aspiration of fluid or tophi to see monosodium urate monohydrate (MSUM) crystals under polarized microscope (needle-shaped, negatively birefringent crystals).
- Serum uric acid (high).

Rheumatoid Hand



Rheumatoid hand

Q: Write down the radiological **findings** of this X-ray.

A: X-ray of both hands in AP view showing:

- Reduction of all joint spaces.
- Periarticular osteopaenia involving metacarpophalangeal and wrist joints of both hands.
- Disorganisation of all proximal interphalangeal (PIP) joints of both hands.
- 'Z'-deformity of thumb.
- Ulnar deviation of both hands.

Q: What is your radiological **diagnosis**?

A: Rheumatoid arthritis

Q: Mention five **bad prognostic factors** of this disease.

A: As follows:

- Higher baseline disability.
- Female gender.
- Involvement of metatarsophalangeal (MTP) joints.
- Positive rheumatoid factor.
- Disease duration of over 3 months.

Q: Mention five **investigations**.

A: As follows:

- CBC with ESR (high ESR, anaemia).
- Rheumatoid arthritis (RA) and Rose–Waaler (RW) tests.
- Anticyclic citrullinated peptide (anti-CCP) antibody (helpful for early diagnosis, highly specific for rheumatoid arthritis).
- X-ray chest [to see diffuse parenchymal lung disease (DPLD), Caplan syndrome].
- C-reactive protein (CRP) (high).

Q: What are the **principles of treatment**?

A: As follows:

- Relief of symptoms: Rest, nonsteroidal anti-inflammatory drug (NSAID), physiotherapy, explanation and reassurance.
- Suppression of activity and progression of disease by disease-modifying antirheumatic drugs (DMARDs) (methotrexate, sulphasalazine, hydroxychloroquine, leflunomide, etc.).
- Biological agents (rituximab, tocilizumab, etc.).
- Restoration of function of affected joints.

Resorption of Terminal Phalanges



Resorption of terminal phalanges

Q: What are your radiological **findings**?

A: X-ray of both hands in AP view showing:

- Periarticular osteopaenia.
- Tapering of terminal phalanges.
- Resorption of distal phalanges of fingers.
- There is calcification at the tip of left index and right thumb.

Q: What is your probable **diagnosis**?

A: Systemic sclerosis.

Q: What is the likely **cause** in this case?

A: CRST or CREST syndrome.

Rickets



Fig. A: Rickets

Q: Write down the radiological **findings** of the X-ray shown in Figure A.

A: X-ray of both hands in AP view showing:

- Widening, splaying, cupping and irregularity of metaphysic.
- Distance between epiphysis and metaphysis is increased (zone of provisional calcification is lost).

Q: What is your radiological **diagnosis**?

A: Rickets.

Q: Mention three other **investigations**.

A: As follows:

- X-ray of elbows and knees.
- Serum calcium and phosphate (both are low).
- Serum alkaline phosphatase (high).
- Serum 25-hydroxy proline (low or absent).

Q: How to **treat**?

A: As follows:

- 25-Hydroxycholecalciferol, 50 µg daily or active vitamin D metabolite (1-α-hydroxycholecalciferol), 1–2 µg daily or 1,25 di-hydroxycholecalciferol, 0.25 to 1.5 µg daily.
- **Plus** calcium—500–1000 mg daily. Higher dose may be required in patients with malabsorption.
- Adequate exposure to sunlight.
- Dietary supplement.



Fig. B: Rickets

Q: Write down the radiological **findings** of the X-ray shown in Figure B.

A: X-ray of leg including knee joint and ankle joint showing:

- Widening, splaying, cupping and irregularity of metaphysis.
- Distance between epiphysis and metaphysis is increased (zone of provisional calcification is lost).
- Bowing of tibia and fibula.

Q: What is your radiological **diagnosis**?

A: Rickets.

Scurvy



Scurvy

Q: Write down the radiological **findings** of this X-ray.
A: X-ray of knee including lower end of femur and upper end of tibia–fibula showing:

- Epiphysis as ring-shaped, sclerotic and sharply marginated called Wimberger sign.
- Metaphysis is dense (zone of provisional calcification), giving a white line called Frankel line.
- Beneath this line, there is a lucent zone called Trummerfeld zone.
- At the corner, there is a spur called Pelkan spur.

Q: What is your radiological **diagnosis**?
A: Scurvy.

Q: What are the **causes**?
A: As follows:

- Dietary deficiency—lack of fruits and fresh vegetables in children >2 months of age.
- In infants—delayed weaning, lack of fruit juice, deficiency in the lactating mother.

Q: How to **treat**?
A: As follows:

- Vitamin C, 250 mg—three to four times daily orally.
- Dietary supplements especially fresh fruits (orange, mango, pineapple, guava, etc.) and liver extract.
- Bottle-fed infants should be given fruit juice. Nursing mother should take sufficient vitamin C, which is secreted in the breast milk.

Avascular Necrosis of Femoral Head



Avascular necrosis of the femoral head

Q: Write down the radiological **finding** of this X-ray.
A: X-ray of pelvis in AP view showing:

- Rarefaction and sclerotic small head of left femur.
- Joint space between head and acetabulum is increased.

Q: What is your radiological **diagnosis**?
A: Avascular necrosis of head of left femur (called osteonecrosis).

Q: What is the **presentation**?
A: Pain in the hip and difficulty in walking.

Q: How to **confirm** your diagnoses?
A: As follows:

- X-ray (may be normal in early stage).
- MRI—more confirmatory (100%).
- Bone scan—increased uptake (helpful in early stage).

Q: Mention five **causes**.
A: As follows:

- Prolonged steroid therapy (other drug—prolonged use of heparin).
- Cushing syndrome.
- Osteoporosis.
- Alcohol abuse.
- Collagen disease (SLE, rheumatoid arthritis, systemic sclerosis, vasculitis).

N.B. Other causes are:

- Sickle cell anaemia (and other haemoglobinopathies).
- Exposure to high barometric pressure—in deep sea divers (Caisson disease) and tunnel workers.
- Perthes disease.
- Radiation therapy.
- Post-traumatic.

Endoscopic Retrograde Cholangiopancreatography (ERCP)



ERCP showing *Ascaris lumbricoides* in common bile duct

Q: What are your **findings**?

A: This is an endoscopic retrograde cholangiopancreatography (ERCP) showing a linear translucent shadow within the common bile duct.

Q: What is your **diagnosis**?

A: Round worm in common bile duct.

Q: How does the patient **present**?

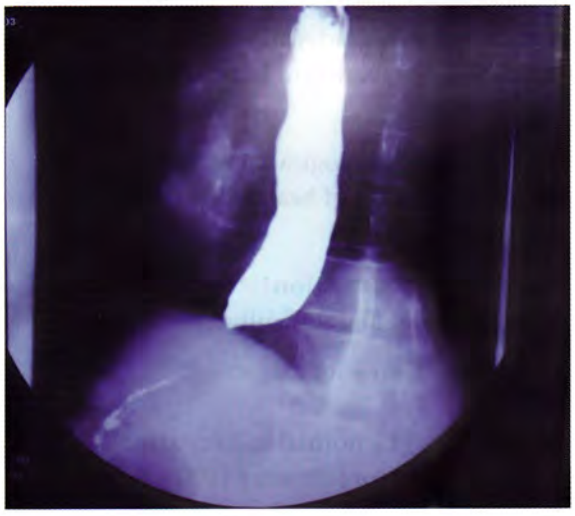
A: As follows:

- Upper abdominal pain, mostly in right hypochondrium.
- Features of obstructive jaundice and cholangitis.

Q: How to **treat** such a case?

A: The worm is removed during ERCP.

Achalasia Cardia



Achalasia cardia

Q: Write down the radiological **finding** of this X-ray.

A: Barium swallow of the oesophagus showing:

- Dilatation of the oesophagus with smooth tapering of its lower end.
- Absence of fundal gas.

Q: What is your radiological **diagnosis**?

A: Achalasia cardia.

Q: Mention one **investigation** to confirm your diagnosis.

A: Oesophageal manometry.

Q: Mention three **complications**.

A: As follows:

- Oesophageal carcinoma.
- Aspiration pneumonia
- Malnutrition.

Q: How to **treat**?

A: As follows:

- Endoscopic dilatation by pneumatic bougie.
- Heller cardiomyotomy.

Carcinoma of Oesophagus



Carcinoma of oesophagus

Q: Write down the radiological **finding** of this X-ray.
A: Barium swallow of the oesophagus showing irregular filling defect at the lower end of oesophagus.

Q: What is your radiological **diagnosis**?
A: Carcinoma of oesophagus.

Q: Mention one investigation to **confirm** your diagnosis.
A: Endoscopy and biopsy.

Carcinoma Stomach



Carcinoma stomach

Q: Write down the radiological **finding** of this X-ray.
A: Barium meal X-ray of stomach showing irregular filling defect at the distal part of stomach.

Q: What is your radiological **diagnosis**?
A: Carcinoma of stomach.

Q: Mention one investigation to **confirm** your diagnosis.
A: Endoscopy and biopsy.

Gastric Outlet Obstruction



Gastric outlet obstruction

Q: Write down the radiological **finding** of this X-ray.
A: Barium meal X-ray of stomach showing:
- Stomach is hugely dilated with food residue.
- Dye is not passing beyond the pylorus.

Q: What is your radiological **diagnosis**?
A: Gastric outlet obstruction.

Q: What is the likely **cause**?
A: Chronic duodenal ulcer with pyloric stenosis.

Q: What other **investigations** do you suggest?
A: Endoscopy and biopsy.

Q: What is the **treatment**?
A: Gastrojejunostomy with vagotomy.

Q: Name one physical **sign**.
A: Visible peristalsis from left to right in upper abdomen.

Q: Mention one **symptom**.
A: Projectile or induced vomiting.

Pancreatic Calcification



Pancreatic calcification

Q: Write down the radiological **finding** of this X-ray.
A: Plain X-ray of abdomen showing multiple calcified shadows superimposed on vertebral column and also on left side along the anatomical distribution of pancreas.

Q: What is your radiological **diagnosis**?
A: Pancreatic calcification.

Q: What is the underlying **diagnosis**?
A: Chronic pancreatitis.

Q: Mention three **causes**.
A: As follows:
- Chronic pancreatitis, commonly alcoholic.
- Fibrocalcific pancreatic disease (FCPD).
- Hereditary pancreatitis.
- Hypercalcaemia due to any cause.
- Haemochromatosis.
- Idiopathic chronic pancreatitis.
- Post-traumatic pancreatitis.

Q: Mention five further **investigations**.
A: As follows:
- Ultrasonogram.
- CT scan or MRI of abdomen.
- Magnetic resonance cholangiopancreatography (MRCP).
- Endoscopic retrograde cholangiopancreatography (ERCP).
- Pancreatic function test.

Polycystic Kidney Disease



Polycystic kidney disease

Q: Write down the radiological **finding** of this X-ray.

A: Intravenous urograms (IVU) showing:

- Enlargement of both kidneys—left one larger than the right.
- Distortion, stretching and elongation of pelvicalyceal system, giving rise to spidery appearance.
- Left ureter is dilated and shifted medially towards the vertebral column.

Q: What is your radiological **diagnosis**?

A: Polycystic kidney disease.

Q: Mention a single **investigation**.

A: Ultrasonography of both kidneys.

Q: If the patient is **unconscious**, what is the likely diagnosis?

A: Subarachnoid haemorrhage (due to rupture of berry aneurysm).

Q: Mention **one treatment**.

A: Ultrasonic-guided aspiration of large cyst.

CT SCAN

CT scan is a radiological procedure that uses X-ray and a computer to produce a series of cross-sectional image of the inside of the body.

Uses:

- To diagnose internal injuries, bleeding, mass lesion, etc.
- To diagnose various rheumatological conditions including bone loss, joint deformity, calcification, etc.
- To guide procedures such as surgery, biopsy and radiation therapy.
- To monitor progression of various diseases like lung nodule, cancer, etc.
- Contrast CT scan is used to assess the vascularity and the nature of a lesion.
- CT angiogram is used to evaluate the vascular system of an organ.

Advantages:

- Higher image resolution than X-ray.
- Noninvasive technique.
- May be used in situations where magnetic resonance imaging (MRI) is contraindicated.
- Cheaper than MRI and many other imaging modalities.
- Quicker than MRI and many other imaging modalities, so it is very useful for quick screening in emergency conditions like subarachnoid haemorrhage.

Advantages of multislice CT over helical CT:

- Increased speed and ability to perform volume acquisition.
- Multislice CT allows faster scanning, thinner sections or larger scan ranges, which lead to less motion artifact, especially in critically ill patients, children and trauma patients.
- Helical CT is a continuous volume acquisition that ensures that no lesions are lost due to respiration or after motion-related artifact. The prime advantage of volume acquisition is the improved three-dimensional capability.

Disadvantages of CT scan:

- Exposure to radiation.
- Reaction to contrast materials if contrast CT scan is performed.
- Image quality is lower than MRI.
- Poor visualization of infarction.

MRI SCAN

MRI is a nonionising imaging technique using magnetic fields and radiofrequency waves to visualize the internal anatomical structures.

Uses:

- To diagnose internal injuries, infarction, mass lesion, etc.
- To diagnose defect with myelination (e.g. multiple sclerosis).
- To diagnose diseases of the spine and spinal cord.
- Contrast MRI is used to assess the vascularity and the nature of a lesion.
- Magnetic resonance angiography (MRA) is used to evaluate the vascular system of an organ.
- Functional MRI (fMRI) of the brain can be used to identify important language and movement control areas in the brain in people who are being considered for brain surgery.

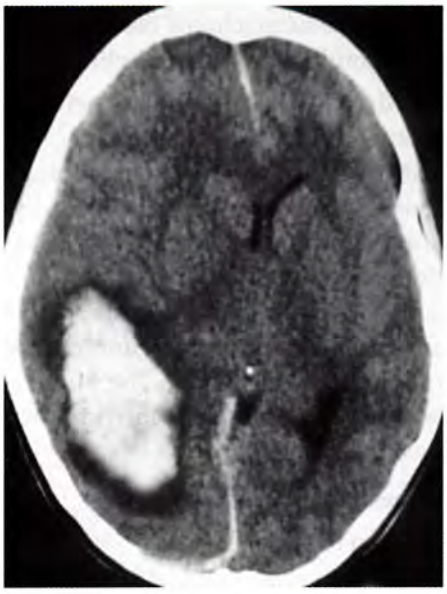
Advantages:

- High-resolution imaging.
- Images of the brain, other cranial structures and the spine are more clear and detailed than with other imaging methods. So MRI is very useful in early diagnosis and evaluation of intracranial and spinal disorders including tumour.
- It enables the detection of abnormalities that might be obscured by bone with other imaging methods.
- Direct multiplanar imaging in transverse, coronal and sagittal planes or in any other desired plane is possible.
- Free from ionizing radiation. So, safe for pregnant women and children.
- Contrast material used in MRI is less likely to produce an allergic reaction than the iodine-based materials used for conventional X-ray and CT scanning.
- Noninvasive technique.

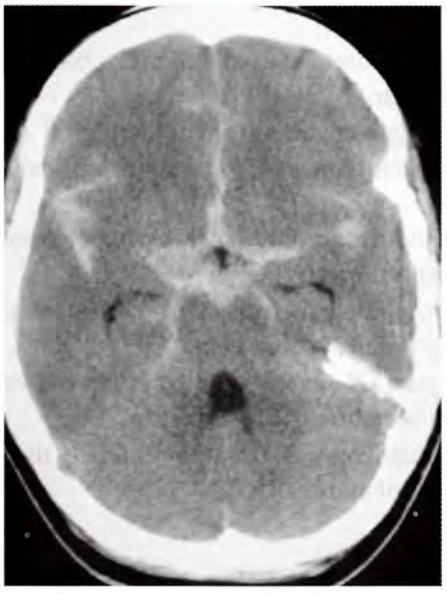
Disadvantages:

- Patient with electronic devices (e.g. cardiac pacemaker, implantable heart defibrillator, etc.), metallic implant (e.g. metallic valve, joint prostheses, etc.) or metallic artificial life support cannot be scanned by MRI due to strong magnetic fields.
- Scanning is time consuming.
- Movement degrades image.
- More expensive.
- Allergic reaction to contrast material may occur rarely (especially in patients with kidney problem who are on dialysis).
- Difficult to perform in claustrophobic patients.

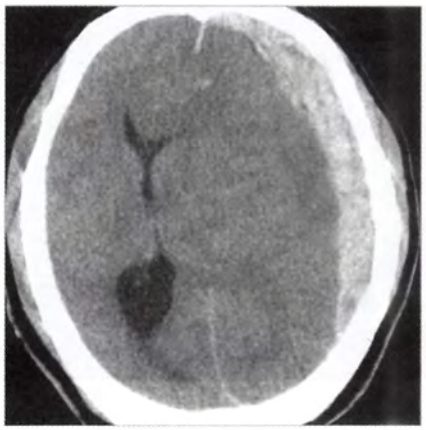
Few Common CT Scans



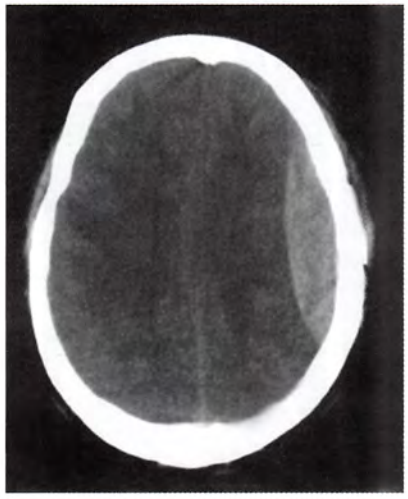
CT scan of the brain shows hyperdense lesion in right parietal lobe with perilesional oedema. The diagnosis is **intracerebral haemorrhage** in right parietal lobe.



CT scan of the head shows high attenuation (white areas) with obliteration of the ventricles. The diagnosis is **subarachnoid haemorrhage**.



CT scan of the head shows crescent-shaped hyperdense extra-cerebral collection within the subdural space. The diagnosis is **subdural haematoma** on the left side.



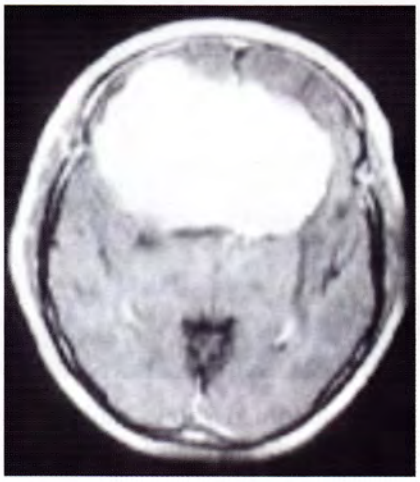
CT scan of the head shows high density bi-convex area. The diagnosis is **extradural haematoma** on the left side.



CT scan of the brain shows hypodense area on the right side with shifting of the ventricle to the left side. The diagnosis is **right-sided cerebral infarction**.



Contrast CT scan of head showing a ring-like cystic hypodense lesion on the right parietal lobe. The diagnosis is **cerebral abscess**.



CT scan of the head shows hyperdense, irregular mass in the frontal region. The diagnosis is **meningioma**.



CT scan of the head shows marked dilatation of both lateral ventricles with thinned brain tissue outside the hypodense area. The diagnosis is **hydrocephalus**.



CT scan of the abdomen shows irregular hypodense mass in the left lobe of the liver. The diagnosis is **hepatoma**.



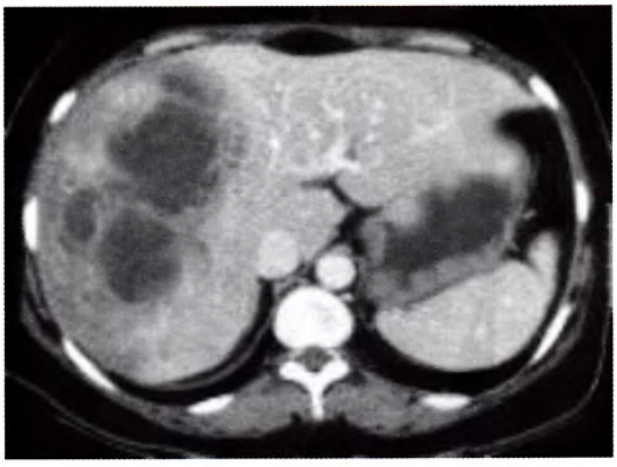
CT scan of the abdomen shows a large hypodense cystic lesion with septation within the right lobe of liver. The diagnosis is **hydatid cyst in liver**.



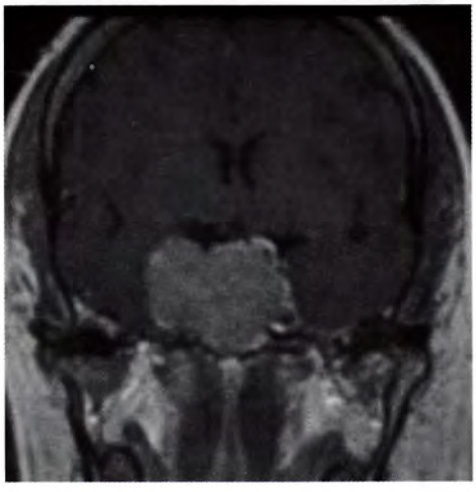
CT scan of the abdomen shows multiple hypodense areas within both right and left lobes of the liver. The diagnosis is **multiple secondaries in liver**.



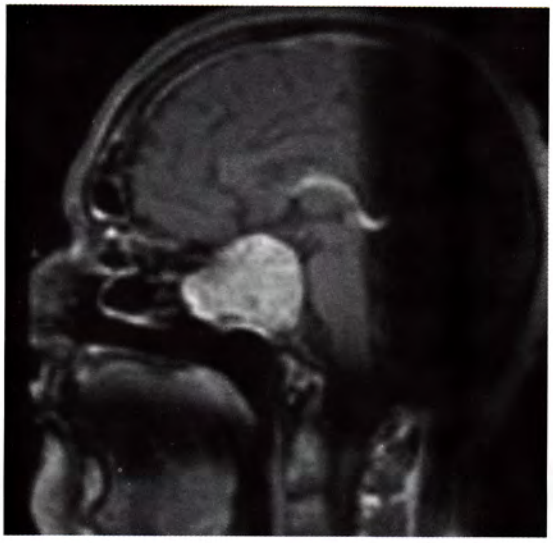
MRI of the dorsolumbar spine lateral view showing destruction of the L2 and L3 vertebral bodies with reduction of joint space. The diagnosis is **Pott disease**.



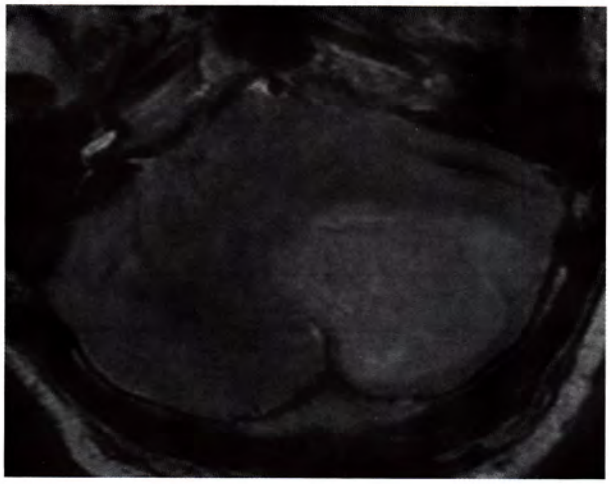
CT scan of the abdomen shows multiple hypodense area with ragged irregular margin within the right lobe of the liver. The diagnosis is multiple **liver abscess**.



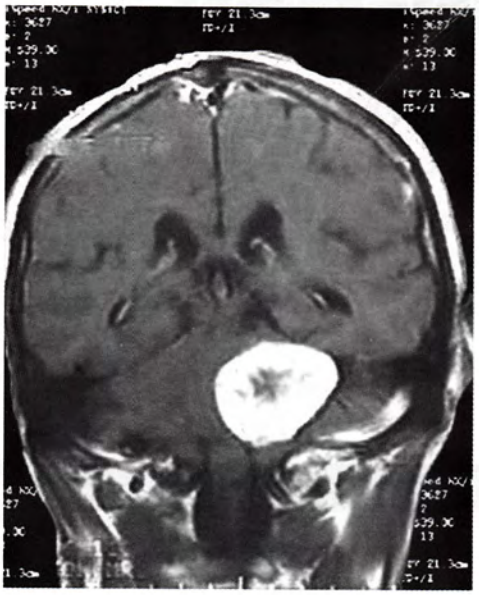
MRI of brain sagittal view shows large irregular hyperdense area in pituitary fossa. The diagnosis is **pituitary macroadenoma**.



MRI of brain coronal view shows large irregular hyperdense area in pituitary fossa. The diagnosis is **pituitary macroadenoma**.



MRI of brain shows large hyperintense mass in the left cerebellar hemisphere. The diagnosis is **cerebellar tumour**.



MRI of the brain showing mixed hyperintense mass in the left cerebellopontine angle. The diagnosis is **acoustic neuroma**.

CHAPTER 15

ECG

"A good start is a good help"

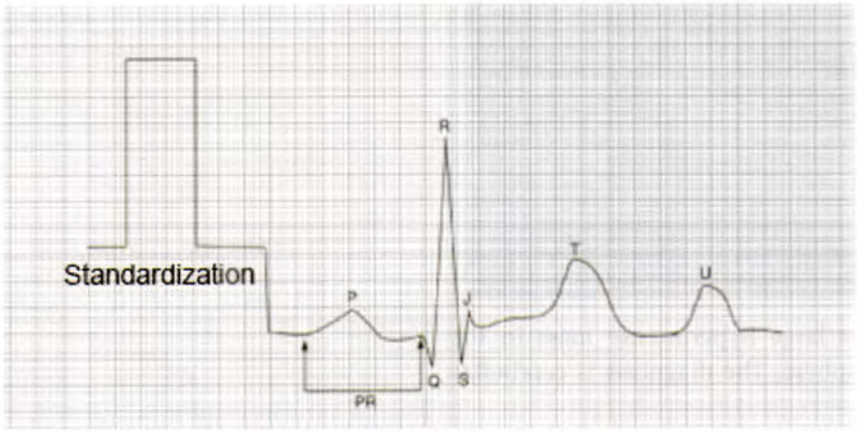
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Basic Concept of ECG

Electrocardiogram (ECG) is the graphical representation of electrical potentials that are produced when the electric current passes through the heart.

Waves in ECG

ECG records the electrical impulse as waves or deflections on ECG paper. One beat is recorded as a group of waves (P–QRS–T).



Waves in ECG tracing

1. P: Represents atrial depolarization.
2. P–R interval: Represents the time taken for the cardiac impulse to spread from SA node to the ventricles.
3. QRS complex: Represents ventricular depolarization.
 - Q(q): First negative deflection before R–wave.
 - R(r): First positive deflection.
 - S(s): Negative deflection after R–wave.
4. T–wave — Represents ventricular repolarization.

Other waves:

1. J: At the beginning of ST-segment.
2. U: Found after T–wave, preceding the next P–wave.

Leads

In a normal ECG recording, there are 12 leads–3 bipolar standard leads, 3 unipolar limb leads and 6 chest leads.

1. **Bipolar standard leads** (limb leads) designated as LI, LII and LIII.
 - LI: Difference of potential between left arm and right arm (LA and RA).
 - LII: Difference of potential between right arm and left leg (RA and LL).
 - LIII: Difference of potential between left arm and left leg (LA and LL).
2. **Unipolar limb leads** (augmented limb leads) designated as augmented vector right (AVr), augmented vector left (AVl) and augmented vector foot (AVf). These leads have very-low voltage that cannot be recorded clearly. So, recordings from these leads are increased in amplitude called augmented unipolar leads.

- AVr: Augmented unipolar right arm (RA) lead. Records the changes of potential occurring in the part of heart facing towards right shoulder.
- AVl: Augmented unipolar left arm (LA) lead. Records the changes of potential of heart facing towards the left shoulder.
- AVf: Augmented unipolar left leg (LL) lead. Records the changes of potential of heart facing towards the left hip.

3. **Chest Leads** (unipolar) Designated by 'V'. Electrodes are placed in the following places on the chest wall:
 - V1: 4th Intercostal space at right sternal border.
 - V2: 4th Intercostal space at left sternal border.
 - V3: Midway between V2 and V4 lead on left side.
 - V4: 5th Intercostal space in left midclavicular line.
 - V5: 5th Intercostal space in left anterior axillary line.
 - V6: 5th Intercostal space in left midaxillary line.

View of the heart in all leads:

- LI, AVl, V5 and V6: Reflects lateral (or anterolateral aspect of heart).
- LII, LIII and AVf: Reflects inferior aspect of heart.
- V1 and V2: Reflects right ventricle.
- V3 and V4: Reflects interventricular septum.
- V5 and V6: Reflects left ventricle.
- V1–V6: Reflects anterior aspect of heart.
- LI, AVl, V1–V6: Reflects extensive anterior aspect of heart or anterolateral.
- LI and AVl: High lateral.
- LII, LIII, AVf, LI, AVl, V5 and V6: Inferolateral.

Interpretation of ECG

Before interpretation one must know details about ECG paper, standardization and different waves in ECG.

Look at the following points carefully:

1. Standardization (see in the beginning): This is 10 mm (1 mV).
2. Paper speed: 25 mm/s.
3. Rhythm: See R–R interval (R–wave to R–wave interval), regular or irregular (LII is called rhythm lead).
4. Count the heart rate.
5. Different waves:
 - P: Normal, small or tall, inverted, wide, notched, bifid, variable configuration.
 - P–R interval: Normal or prolonged or short.
 - Q: Normal or pathological.
 - R: Normal or tall or short, notched or M-pattern.
 - QRS complex: Normal or wide, high or low voltage, variable or change of shape.
 - ST-segment: Elevated or depressed.
 - T: Normal or tall or small or inverted.
 - U-wave: Normal or small.
 - QT: Short or prolonged.
6. Axis: Whether normal or right- or left-axis deviation.
7. Abnormalities: Any arrhythmia, infarction, hypertrophy.

Q: What are the **diseases diagnosed by looking at an ECG?**

A: As follows:

- Tachycardia or bradycardia.
- Chamber enlargement.
- Myocardial infarction.
- Arrhythmias.
- Block [first-degree block, sinoatrial block (SA block), atrioventricular block (AV block), bundle-branch block].
- Drug effect (such as digoxin).
- Extracardiac abnormalities: Electrolyte imbalance (such as hypokalaemia or hyperkalaemia), hypo- or hypercalcaemia, low-voltage tracing (in myxedema, hypothermia, emphysema).
- Exercise ECG to see coronary artery disease.

ECG Paper

ECG paper shows small and large squares. In each small square, thin horizontal and vertical lines are present at 1-mm interval. A heavier, thick line is present at every 5-mm (5 small squares) interval. Time is measured horizontally and height is measured vertically.

1. One small square:
 - Height = 1 mm.
 - Horizontal (in time) = 0.04 s.
2. One big square (5 small squares):
 - Height = 5 mm.
 - Horizontal (in time) = 0.04 × 5 s = 0.2 s.

 So, 0.2 s = 5 mm.
 1 s = 5/0.2 = 25 mm.
 So, recording speed is 25 mm/s. (i.e. 1500 mm/min).
3. Isoelectric line: It is the base line in ECG paper. Waves are measured either above (positive deflection) or below (negative deflection).

Standardization of ECG

- Normally, 1-mv current: 10-mm height (10 small squares).
- Half strength: 5 mm.
- Recording speed: 25 mm/s (i.e. 1500 mm/min).

Before telling **low voltage or high voltage,** see the normal standardization (i.e. 10 mm in height).

Criteria of low-voltage tracing:

- In standard limb leads: QRS complex <5 mm (mainly R-wave).
- In chest leads: QRS complex <10 mm (mainly R-wave).

Remember the following points:

- Depolarization indicates initial spread of stimulus through the muscle, causing activation or contraction.
- Repolarization indicates return of stimulated muscle to the resting state (recovery from activation or contraction).
- Depolarization towards the electrode: Positive deflection (above the isoelectric line).
- Depolarization away from the electrode: Negative deflection (below the isoelectric line).
- Rhythm: Interval between two successive RR.

Normal ECG

Characteristics of normal ECG:

- Normal ECG consists of P-wave (atrial beat), followed by QRS complex, ST- and T-wave (ventricular beat).
- Capital letter P, Q, R, S, T: Indicates large wave (>5 mm).
- Small letter p, q, r, s, t: Indicates small wave (<5 mm).

Intervals and segment in ECG

- P-R interval: Distance between the beginning of P and beginning of QRS (Q).
- P-P interval: Distance between two successive P-waves. In sinus rhythm, P-P interval is regular.
- R-R interval: Distance between two successive R-waves.
- Q-T interval: Distance interval between the beginning of Q-wave and the end of T-wave.
- S-T segment: Distance from the end of QRS complex to the beginning of T-wave. It indicates the beginning of ventricular repolarization. Normally, it is in isoelectric line, but may vary from –0.5 to +2 mm in chest leads.

Details of Waves and Intervals

P-Wave

Characters of normal P-wave:

- P-wave is better seen in LII (also seen in V1).
- Normal P is rounded–neither peaked nor notched.
- Width or duration (in time, horizontally): 0.10 s (2.5 small sq.).
- Height: 2.5 mm (2.5 small squares) height × duration = 2.5 × 2.5 small squares.
- P-wave is upright in all leads, mainly LI, LII and AVf (except AVr. P is inverted in AVr and occasionally in AVl).
- P-wave in V1 may be biphasic (equal upward and downward deflection), notched and wide (activation of right atrium produces positive component and activation of left atrium produces negative component).

Abnormalities of P-wave: It may be absent, tall or small, wide, notched, biphasic, inverted, variable, multiple.

Causes of absent P-wave:

- Atrial fibrillation (P is absent or replaced by fibrillary **f**-wave).
- Atrial flutter (P is replaced by flutter wave, which shows **saw-tooth** appearance).
- Sinoatrial (SA) block or sinus arrest.
- Nodal rhythm (usually abnormal, small P-wave).
- Ventricular ectopic and ventricular tachycardia.
- Supraventricular tachycardia (P-wave is hidden within QRS complex, due to tachycardia).
- Hyperkalaemia.
- Idioventricular rhythm.

Causes of tall P-wave:

- Tall P-wave is called P-pulmonale (height > 2.5 mm, i.e. > 2.5 small squares).
- It is due to right atrial hypertrophy or enlargement.

Causes of small P-wave:

- Atrial tachycardia.
- Atrial ectopic.
- Nodal rhythm (high nodal).
- Nodal ectopic (high nodal).

Causes of wide P-wave:

- Broad and notched P-wave is called P-mitrale (duration > 0.11 s or > 2.5 small squares).
- It is due to left atrial hypertrophy or enlargement.
- In V1, P-wave may be biphasic with a small positive wave preceding a deep and broad negative wave (indicates left atrial enlargement or hypertrophy).

Causes of inverted P-wave (negative in LI, LII and AVf):

- Incorrectly placed leads (reversed arm electrodes).
- Dextrocardia.
- Nodal rhythm with retrograde conduction.
- Low atrial and high nodal ectopic beats.

Causes of variable P-waves:

- Presence of variable P-waves indicates wandering pacemaker.

Causes of multiple P-waves (consecutive two or more):

- AV block (either partial or complete heart block).
- Supraventricular tachycardia (SVT) with AV block.

P-R Interval

Characters of normal P-R interval:

- Normal P-R interval: 0.12–0.20 s (maximum five small squares).
 - In children, upper limit is 0.16 s.
 - In adolescent, upper limit is 0.18 s.
 - In adult, upper limit is 0.22 s.
- PR interval is short, if it is < 0.10 s; and long, if it is >0.22 s.

Abnormalities of P-R Interval: It may be prolonged, short and variable.

Prolonged P-R interval (>0.2 s): It is due to first-degree heart block. Causes are:

- Ischaemic heart disease (occasionally, inferior myocardial infarction).
- Acute rheumatic carditis.
- Myocarditis (due to any cause).
- Atrial dilatation or hypertrophy.
- Hypokalaemia.
- Drugs: Digitalis toxicity, quinidine, occasionally β-blocker, calcium channel blocker (verapamil).

Short P-R interval (<0.12 s): Causes are—

- Wolff-Parkinson-White (WPW) syndrome: In this case, there is δ-wave.
- Lown-Ganong-Levine (LGL) syndrome: In this case, there is no δ-wave.
- Nodal rhythm.
- Nodal ectopic (high nodal).
- Occasionally, if dissociated beat is present and also in infant, steroid therapy.

Variable P-R interval: Causes are—

- Wenckebach phenomenon (Mobitz type I): There is progressive lengthening of P-R interval followed by a drop beat.
- Partial heart block (Mobitz type II): P-R interval is fixed and normal, but sometimes P-wave is not followed by QRS complex.
- 2:1 AV block: Alternate P-wave is not followed by QRS complex.
- Complete AV block: No relation between P-wave and QRS complex.
- Wandering pacemaker: Variable configuration of P-wave.

Q-Wave

Characters of normal Q-wave:

- Q-wave is usually absent in most of the leads. However, small Q-wave may be present in I, II, AVl, V5 and V6. This is due to septal depolarization.
- Small q may be present in LIII (which disappears with inspiration).
- Depth: <2 mm (2 small squares).
- Width: One small square.
- It is 25% or less in amplitude of the following R-wave in the same lead.

Characters of pathological Q-wave:

- Deep >2 mm (2 small squares).
- Wide > 0.04 s or more (>1 mm or 1 small square).
- Should be present in more than one lead.
- Associated with loss of height of R-wave.
- Q-wave should be >25% of the following R-wave of the same lead.

Causes of pathological Q-wave:

- Myocardial infarction (commonest cause).
- Ventricular hypertrophy (left or right).
- Cardiomyopathy.
- LBBB.
- Emphysema (due to axis change or cardiac rotation).
- Q-wave only in LIII is associated with pulmonary embolism (SI, QIII and TIII pattern).

N.B. Remember the following points:

- Q-wave in V1, V2 and V3 may be seen in left ventricular hypertrophy (LVH), confused with old myocardial infarction.
- Abnormal Q-wave in LIII may be found in pulmonary embolism.
- Abnormal Q-wave in LIII and AVf may be found in Wolff-Parkinson-White syndrome (WPW syndrome) (confuses with old inferior myocardial infarction).

R-Wave

Characters of normal R-wave:

- Duration <0.01 s.
- R-wave is usually small (<1 mm) in V1 and V2. It increases progressively in height in V3–V6 (tall in V5 and V6).

Normal height of R-wave (If R-wave is >25 mm, it is always pathological):

- AVl <13 mm.
- AVf <20 mm.
- V5 and V6 <25 mm.

Abnormalities of R-wave: It may be tall, small, poor progression.

Causes of tall R-wave:

1. Left ventricular hypertrophy (in V5 or V6 >25 mm, AVl >13 mm, aVf >20 mm).
2. In V1, tall R-wave may be due to:
 - Normal variant.
 - Right ventricular hypertrophy (RVH).
 - True posterior myocardial infarction.
 - WPW syndrome (type A).
 - Right bundle branch block (RBBB).
 - Dextrocardia.

Causes of small R-wave: Looks like low-voltage tracing.

- Incorrect ECG calibration (standardization).
- Obesity.
- Emphysema.
- Pericardial effusion.
- Hypothyroidism.
- Hypothermia.

R-wave progression: The height of R-wave gradually increases from V1 to V6. This phenomenon is called R-wave progression.

Poor progression of R-wave: Normally, amplitude of R-wave is tall in V5 and V6. In poor R-wave progression, amplitude of R-wave is progressively reduced in V5 and V6. Causes are:

- Anterior or anteroseptal myocardial infarction.
- Left bundle branch block (LBBB).
- Left ventricular hypertrophy (though R-wave is tall in most cases).
- Dextrocardia.
- Cardiomyopathy.
- Chronic obstructive pulmonary disease (COPD).
- Left-sided pneumothorax.
- Left-sided pleural effusion (massive).
- Marked clockwise rotation.
- Chest electrodes placed incorrectly.
- Deformity of the chest wall.
- Normal variation.

S-Wave

Characters of normal S-wave:

- Normally, deep in V1 and V2.
- Progressively diminished from V1 to V6.
- In V3, R- and S-waves are almost equal (correspond with interventricular septum).

QRS Complex

Characters of normal QRS complex:

- QRS complex is predominantly positive in L1, AVl, V5 and V6.
- It is negative in AVr, V1 and V2.
- In V1, S-wave is greater than R-wave, and in V5 and V6, R-wave is tall.
- Normal duration of QRS complex is 0.08–0.11 s (<3 small squares) and height < 25 mm.

Abnormalities of QRS complex: It may be of high voltage, low voltage, wide, may change in shape and be variable.

Causes of high-voltage QRS complex:

- Incorrect calibration.
- Thin chest wall.
- Ventricular hypertrophy (right or left or both).
- WPW syndrome.
- True posterior myocardial infarction (in V1 and V2).

Causes of low-voltage QRS complex (<5 mm in LI, LII, LIII and <10 mm in chest leads):

- Incorrect calibration.
- Thick chest wall or obesity.
- Hypothyroidism.
- Pericardial effusion.
- Emphysema.
- Chronic constrictive pericarditis.
- Hypothermia.

Causes of wide QRS complex (>0.12 s, 3 small squares):

- Bundle branch block (LBBB or RBBB).
- Ventricular ectopics.
- Ventricular tachycardia.
- Idioventricular rhythm.
- Ventricular hypertrophy.
- Hyperkalaemia.
- WPW syndrome.
- Pacemaker (looks like LBBB with spike).
- Drugs (quinidine, procainamide, phenothiazine, tricyclic antidepressants).

Causes of changes in shape of QRS complex:

- Right or left bundle branch block (slurred or M-pattern).
- Ventricular tachycardia.
- Ventricular fibrillation.

- Hyperkalaemia.
- WPW syndrome.

Causes of variable QRS complex:

- Multifocal ventricular ectopics.
- Torsades de pointes.
- Ventricular fibrillation.

ST Segment

Characters of normal ST segment:

- Normally, it is in isoelectric line (lies at same level of ECG baseline).
- ST elevation is normal up to 1 mm in limb leads and 2 mm in chest leads (mainly V1–V3).
- Normally, ST segment may be depressed, <1mm.

Abnormalities of ST segment: It may be elevated or depressed.

Causes of ST elevation (>2 mm):

- Recent myocardial infarction (ST elevation with convexity upward).
- Acute pericarditis (ST elevation with concavity upward, chair shaped or saddle shaped).
- Prinzmetal angina (ST elevation with tall T-wave).
- Ventricular aneurysm (persistent ST elevation).
- Early repolarization (high take off).
- Normal variant in Africans and Asians.
- May be in hyperkalaemia.

Causes of ST depression (below the isoelectric line):

- Acute myocardial ischaemia (horizontal or down slope ST depression with sharp angle ST–T junction).
- Ventricular hypertrophy with strain (ST depression with convexity upward and asymmetric T inversion).
- Digoxin toxicity (sagging of ST depression—like thumb impression, also called reverse tick).
- Acute true posterior myocardial infarction (in V1 and V2), associated with dominant R- and tall upright T-wave.

T-Wave

Characters of normal T-wave:

- Upright in all leads, except AVr.
- Usually, more than 2 mm in height.
- May be normally inverted in V1 and V2.
- Normally, not more than 5 mm in standard leads and 10 mm in chest leads.
- Minimum one-fourth of R-wave of the same lead.
- Tip of T-wave is smooth (rounded).

Abnormalities of T-wave: It may be inverted, tall, peaked, tented.

Causes of T inversion:

- Myocardial ischaemia and infarction.
- Subendocardial myocardial infarction (non-Q-wave myocardial infarction).
- Ventricular ectopics.
- Ventricular hypertrophy with strain.
- Acute pericarditis.
- Cardiomyopathy.
- Myxoedema.
- Bundle branch block.
- Drugs (digitalis, emetine, phenothiazine).
- Physiological (smoking, anxiety, anorexia, exercise, after meal or glucose).

Causes of tall, peaked T-wave:

- Hyperkalaemia (tall, tented or peaked).
- Hyperacute myocardial infarction (tall T-wave).
- Acute true posterior myocardial infarction (tall T-wave in V1–V2).
- May be normal in some Africans and Asians.

Causes of small T-wave:

- Hypokalaemia.
- Hypothyroidism.
- Pericardial effusion.

U-Wave

Characters of normal U-wave:

- It is better seen in chest leads (V2–V4).
- Normal amplitude is 1 mm (2 mm in athlete).

Abnormalities of U-wave: It may be inverted or prominent.

Causes of inverted U-wave:

- Ischaemic heart disease.
- Left ventricular hypertrophy with strain (hypertensive heart disease).

Causes of prominent U-wave:

- May be normally present (usually small).
- Hypokalaemia (commonest).
- Bradycardia.
- Ventricular hypertrophy.
- Hyperthyroidism.
- Hypercalcaemia.
- Drugs (phenothiazine, quinidine, digitalis).

N.B. Large U-wave may cause torsades de pointes.

Q-T Interval

Characters of normal Q–T interval:

- Normal Q–T interval is 0.35–0.43 s.
- Its duration varies with heart rate, becoming shorter as the heart rate increases and longer as the heart rate decreases.
- It is better seen in AVl (because there is no U-wave).

Abnormalities of Q–T interval: It may be short or long.

Causes of short Q–T interval:

- Digoxin effect.
- Hypercalcaemia.
- Hyperthermia.
- Tachycardia

Causes of long Q–T interval:

- Hypocalcaemia.
- Bradycardia.
- Acute myocarditis.
- Acute myocardial infarction.
- Hypothermia.
- Drug (quinidine, procainamide, flecainide, amiodarone, tricyclic antidepressant, disopyramide, pentamidine).
- Cerebral injury (head injury, intracerebral haemorrhage).
- Hypertrophic cardiomyopathy.
- During sleep.
- Hereditary: Jervell and Lange–Nielsen syndrome, Romano–Ward syndrome.

Rhythm of Heart

To see the rhythm—see the successive R–R interval.

- If the R–R interval is equal, it is called regular rhythm.
- If the R–R interval is irregular, then it is called irregular rhythm.

Causes of irregular rhythm

1. Physiological: Sinus arrhythmia.
2. Pathological:
 - Atrial fibrillation.
 - Atrial flutter.
 - Ectopic beat.
 - SA block or sinus arrest.
 - Atrial tachycardia with block.
 - Second-degree heart block.
 - Ventricular fibrillation.

Characters of sinus rhythm: It shows the following five characters:

- P–wave is of sinus origin (means characters of normal P–wave).
- P–waves and QRS complexes are regular (which means P–P and R–R interval should be constant and identical).
- Constant P–wave configuration in a given lead.
- P–R interval and QRS interval should be within normal limit.
- Rate should be between 60 and 100 beats/min (atrial and ventricular rates are identical).

Q: What is arrhythmia?

A: It is the abnormality in initiation or propagation of cardiac impulse.

Calculation of Heart Rate

Methods vary according to the cardiac rhythm, whether regular or irregular. Heart rate is the number of beats/min. In the ECG paper:

- 0.04 s = 1 small square.
- 0.2 s = 5 small squares or 1 large square.
- So, 1 s = 25 small squares or 5 large squares.
- So, 1 min = 25 × 60 = 1500 small squares or 5 × 60 = 300 large squares.

Heart rate is determined in the following way:

1. **When the cardiac rhythm is regular:**
 - Calculate the R–R or P–P interval in small squares or large squares (if the rhythm is sinus, R–R or P–P interval is same).
 - If small square is calculated, heart rate is = 1500/(small squares between R–R interval or P–P interval).
 - If large square is calculated, heart rate is = 300/(large squares between R–R interval or P–P interval).
2. **When the rhythm is irregular:**
 - Count the number of R–waves in 30 large squares (it is equivalent to 6 s).
 - Then simply multiply this by 10 (it becomes rate in 1 min).

Cardiac Axis

Definition: It is the sum of all the depolarization waves as they spread through the ventricles as seen from the front.

Axis determination

- It can be derived easily from the amplitude of QRS complex in LI, LII and LIII.
- Greatest amplitude of R-wave in LI or LII or LIII indicates the proximity of cardiac axis to that lead.
- Axis lies at 90° to the isoelectric complex, i.e. positive and negative deflections are equal in any of the lead LI, LII, LIII, AVl, AVr and AVf.

Normal axis is between −30° and +90°.

Quick and simple way of determination of cardiac axis:

- Positive QRS complex in both LI and LII means axis is normal.
- Positive QRS complex in LI and negative in LIII (tall R-wave in LI and deep S-wave in LIII)–means left-axis deviation.
- Negative QRS complex in LI and positive in LIII (tall R in LIII and deep S in LI)—means right-axis deviation.

Left-axis deviation: When the cardiac axis is between −30°and −90°. Causes are:

- Normal variant (with advanced age).
- Left ventricular hypertrophy.
- Left anterior hemiblock.
- Left bundle branch block.
- Inferior myocardial infarction.
- T-wave from apex of left ventricle.
- WPW syndrome (some).
- Pacing from the apex of the right or left ventricle (endocardial pacing).
- Emphysema.

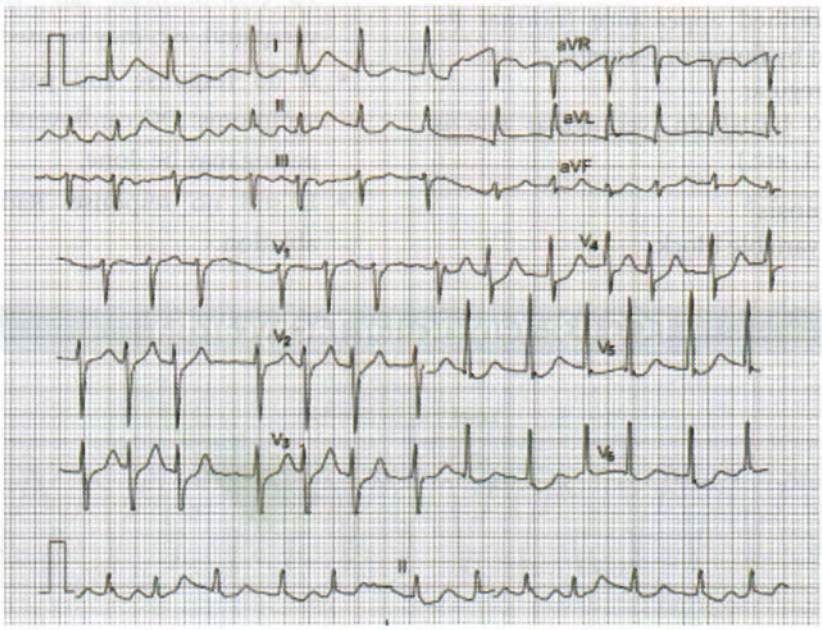
Right-axis deviation: When the cardiac axis is between +90° and +180°. Causes are:

- Normal variant (common in children and young adult).
- Right ventricular hypertrophy (due to any cause such as—chronic cor pulmonale, pulmonary embolism, congenital heart diseases, i.e. tetralogy of Fallot).
- Anterolateral myocardial infarction (high lateral MI).
- Left posterior hemiblock.
- Dextrocardia.
- WPW syndrome (type A).
- Right bundle branch block.
- Epicardial pacing.

Thumb signs
III ↓ LAD
III ↑ RAD

Some Common ECG Tracings

ECG 01: Atrial Fibrillation



Atrial fibrillation

Q: Write down three important **abnormal findings** in this ECG.

A: As follows:

- P–wave is absent.
- Rhythm is irregularly irregular (R–R interval is irregular).
- There are fibrillary waves.

Q: What is the **heart rate**?

A: 125/min.

Q: What is your **diagnosis**?

A: Atrial fibrillation.

Q: Write down five important **causes**.

A: As follows:

- Chronic rheumatic heart disease, usually with mitral stenosis.
- Acute myocardial infarction.
- Thyrotoxicosis.
- Hypertension.
- Lone atrial fibrillation (AF).

Q: Write down two important **complications**.

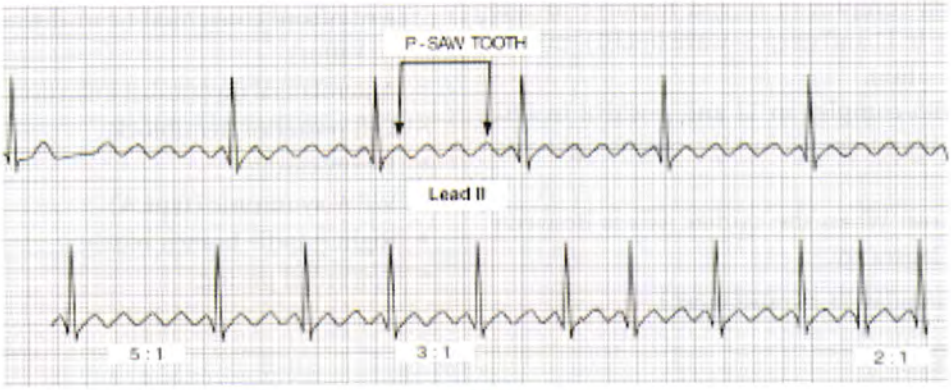
A: As follows:

- Thromboembolism (systemic and pulmonary).
- Heart failure.

Q: If the patient is asymptomatic, mention simple **management**.

A: Low-dose aspirin should be given to prevent thromboembolism.

ECG 02: Atrial Flutter



Atrial flutter

Q: Write down three important **abnormal findings** in this ECG.

A: As follows:

- P wave: Saw-toothed appearance (normal P–wave is replaced by flutter or F-wave).
- R–R interval: Irregular.
- Atrial rate: 300 beats/min, ventricular rate is variable (2:1, 3:1, etc.).

Q: What is your **diagnosis**?

A: Atrial flutter with variable block.

Q: How to **treat**?

A: As follows:

- To control heart rate: Digoxin, β-blocker or verapamil, etc. may be used.
- If no response and patient has troublesome symptoms: DC cardioversion or atrial overdrive pacing may be done.
- If still no response: Radiofrequency catheter ablation.

ECG 03: Ventricular Tachycardia



Ventricular tachycardia

Q: Write down three important **abnormal findings** in this ECG.

A: As follows:

- P-wave: Absent.
- QRS complex: Broad >0.14 s (abnormal or bizarre pattern).
- Ventricular rate: 130 beats/min.

Q: What is your **diagnosis**?

A: Ventricular tachycardia.

Q: Mention two **differential** diagnoses.

A: As follows:

- Supraventricular tachycardia with right bundle branch block.
- Supraventricular tachycardia with WPW syndrome.

Q: Mention five **causes**.

A: As follows:

- Acute myocardial infarction.
- Myocarditis.
- Cardiomyopathy.
- Ventricular aneurysm.
- Electrolyte imbalance (mainly hypokalaemia and hypomagnesaemia).

ECG 04: Acute Myocardial Infarction

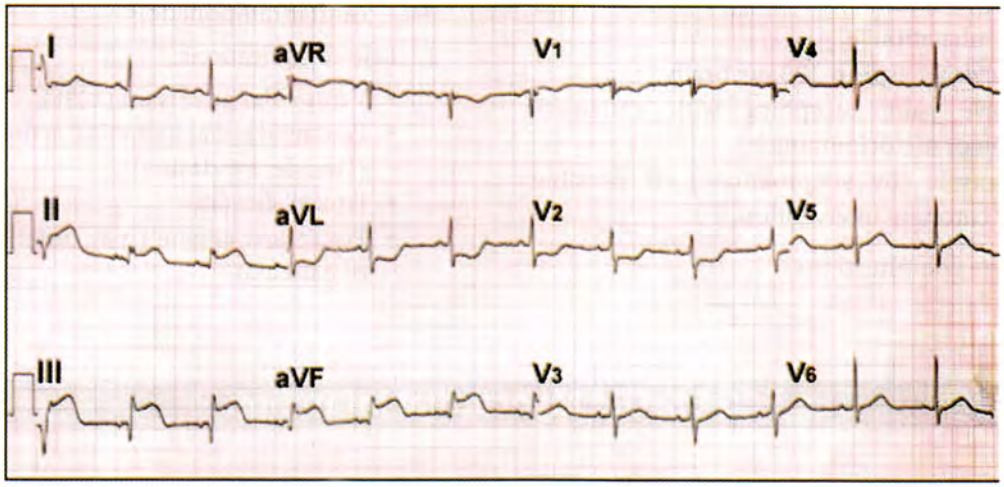


Fig. A: Acute inferior myocardial infarction

Q: Write down two important **abnormal findings** in the ECG shown in Figure A.

A: As follows:

- ST elevation in II, III and AVf.
- ST depression with inverted T-wave in I, AVl and V2.

Q: What is your **diagnosis**?

A: Acute inferior myocardial infarction.

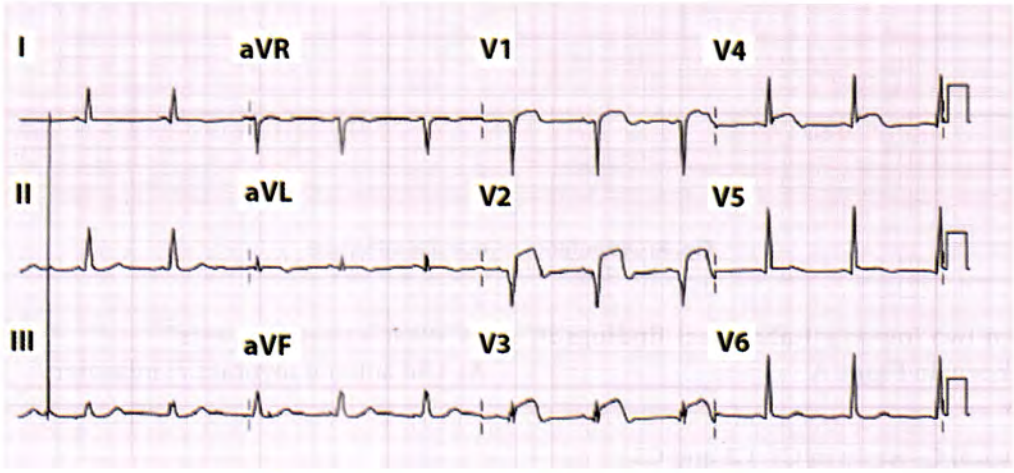


Fig. B: Acute anteroseptal myocardial infarction

Q: Write down two important **abnormal findings** in the ECG shown in Figure B.

A: As follows:

- ST elevation in V1, V2 and V3.
- Pathological Q-waves in V1 and V2.

Q: What is your **diagnosis**?

A: Acute anteroseptal myocardial infarction.

Q: Mention two **investigations**.

A: As follows:

- Serum troponin I.
- Serum CK-MB.

Q: Write down **immediate management** plan.

A: As follows:

- Complete bed rest.
- Oxygen inhalation.
- Tab. Chewable aspirin 300 mg orally.
- To relieve pain: Morphine with antiemetic (cyclizine or metoclopramide).
- Thrombolysis (by streptokinase). If possible, primary coronary intervention.

Q: What are the **complications**?

A: As follows:

1. Early complications:
 - Arrhythmia: Ventricular ectopics (more common), ventricular fibrillation, ventricular tachycardia, sinus bradycardia [common in inferior myocardial infarction (MI)], sinus tachycardia, atrial fibrillation, heart block.
 - Cardiogenic shock.
 - Cardiac failure [left ventricular failure (LVF), biventricular failure].
 - Acute pericarditis (common in 2nd or 3rd day).
 - Thromboembolism (systemic and pulmonary).
 - Rupture of the papillary muscle or chordae tendineae resulting in mitral regurgitation.
 - Rupture of interventricular septum, causing VSD.
 - Rupture of the ventricular wall leading to cardiac tamponade.
2. Late complications:
 - Ventricular aneurysm (10%).
 - Postmyocardial infarction syndrome (Dressler syndrome).
 - Frozen shoulder.
 - Postinfarct angina (may occur in up to 50% of patients).

ECG 05: Old Myocardial Infarction

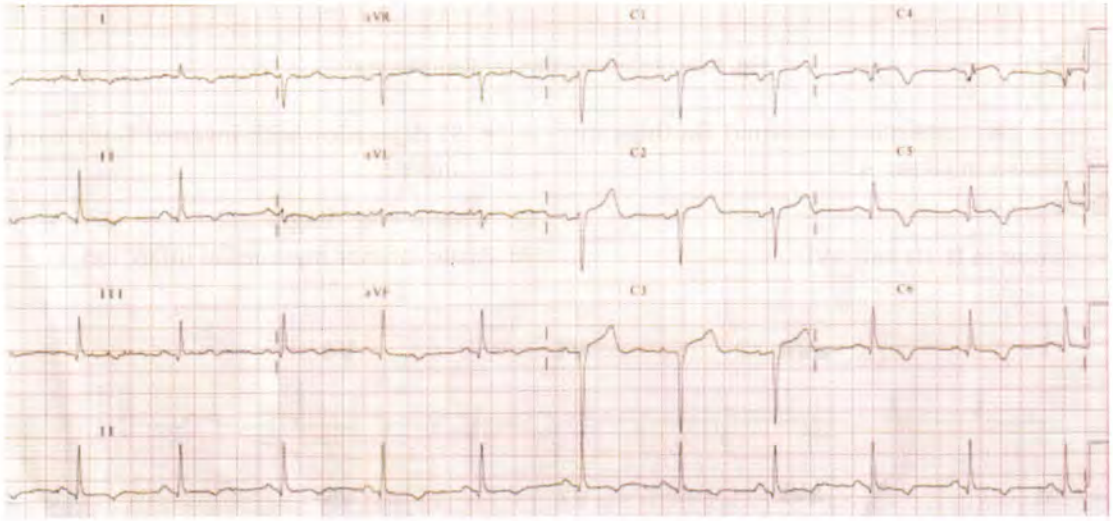


Fig. A: Old anterior myocardial infarction

Q: Write down two important **abnormal findings** in the ECG shown in Figure A.

A: As follows:

- Pathological Q-waves in C1, C2 and C3.
- T inversion in C4, C5 and C6.

Q: What is your **diagnosis**?

A: Old anterior myocardial infarction.

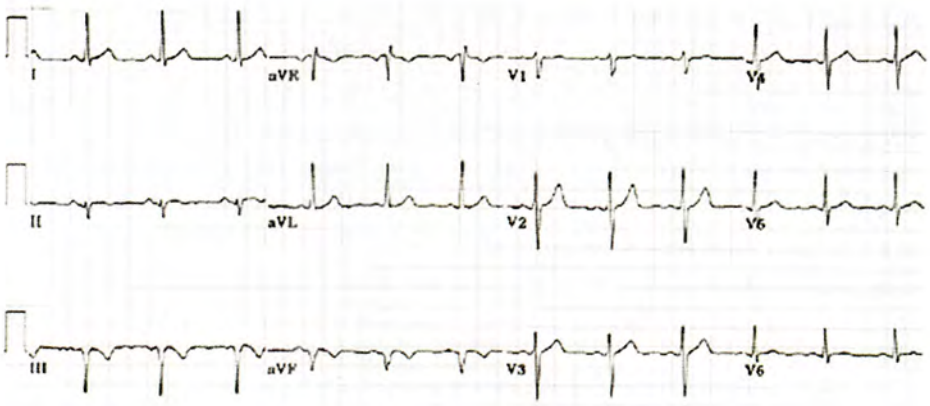
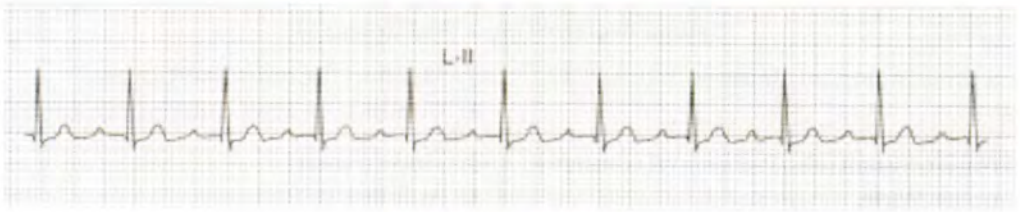


Fig. B: Old inferior myocardial infarction

Q: What is the **abnormal finding** in the ECG shown in Figure B?
A: Pathological Q-wave in II, III and AVf.

Q: What is your **diagnosis**?
A: Old inferior myocardial infarction.

ECG 06: First-Degree AV Block



First-degree AV block

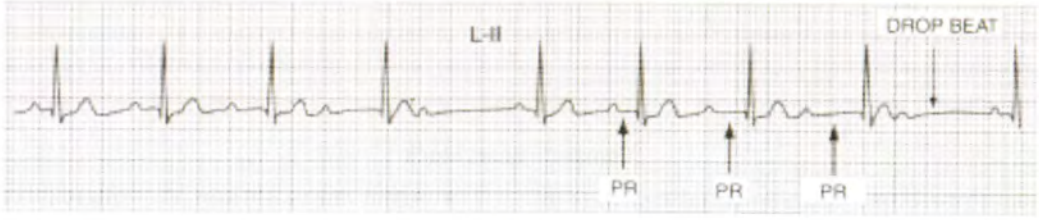
Q: What is the abnormal **finding** in this ECG?
A: P–R interval is prolonged >0.22 s (normal 0.12–0.20 s).

Q: What is your diagnosis?
A: First-degree AV block.

Q: Mention four **causes**?
A: As follows:

- Digoxin toxicity.
- Acute myocardial infarction (common in inferior myocardial infarction).
- Acute rheumatic carditis.
- Hyperkalaemia.

ECG 07: Second-Degree AV Block (Mobitz Type I)



Second-degree AV block (Mobitz type I)

Q: Write down two important **abnormal findings** in this ECG.

A: As follows:

- Progressive lengthening of P–R interval followed by absent QRS complex (one P is not followed by a QRS complex).
- R–R interval: Irregular (progressive shortening of R–R interval until block occurs).

Q: What is your **diagnosis**?

A: Second-degree AV block, Mobitz type I (Wenckebach phenomenon).

Q: Mention three **causes**?

A: As follows:

- Physiological: Athlete, during rest, sleep (due to increased vagal tone).
- Drugs: Digoxin toxicity.
- Acute myocardial infarction (commonly inferior myocardial infarction).

Q: Where is the **lesion**?

A: The block is in the higher area of AV node (proximal to bundle of His).

Q: What is the **prognosis**?

A: Good prognosis.

ECG 08: Second-Degree AV Block (Mobitz Type II)



Second-degree AV block (Mobitz type II)

Q: Write down three important **findings** in this ECG.

A: As follows:

- P–R interval is constant (also P–P interval constant).
- QRS complex: Wide.
- Alternate P-wave is conducted.

Q: What is your **diagnosis**?

A: Mobitz type II second-degree AV block with 2:1 conduction.

Q: What are the **complications**?

A: As follows:

- Complete heart block.
- Stokes–Adams syndrome.
- Heart failure.

Q: Where is the **lesion**?

A: Disease of His–Purkinje system.

Q: Mention the most **likely cause.**

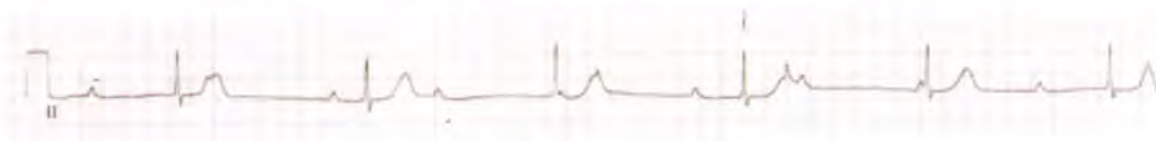
A: Common in acute anterior myocardial infarction.

Q: How to **treat**?

A: As follows:

1. When associated with acute inferior myocardial infarction:
 - If asymptomatic—close monitoring and follow-up.
 - If symptomatic—Inj. atropine 0.6 mg intravenous (IV). If no response, temporary pacemaker. Majority will resolve in 7–10 days.
2. If associated with acute anterior myocardial infarction—temporary pacing followed by permanent pacemaker (because complete heart block may develop).

ECG 09: Complete Heart Block



Complete heart block

Q: Write down three important **abnormal findings** in this ECG.

A: As follows:

- Atrial rate is 60/min, P–P interval is constant.
- Ventricular rate is 35/min.
- There is no relationship between P-wave and QRS complex

Q: What is your **diagnosis**?

A: Complete heart block.

Q: Write down three findings you expect in CVS **examination**.

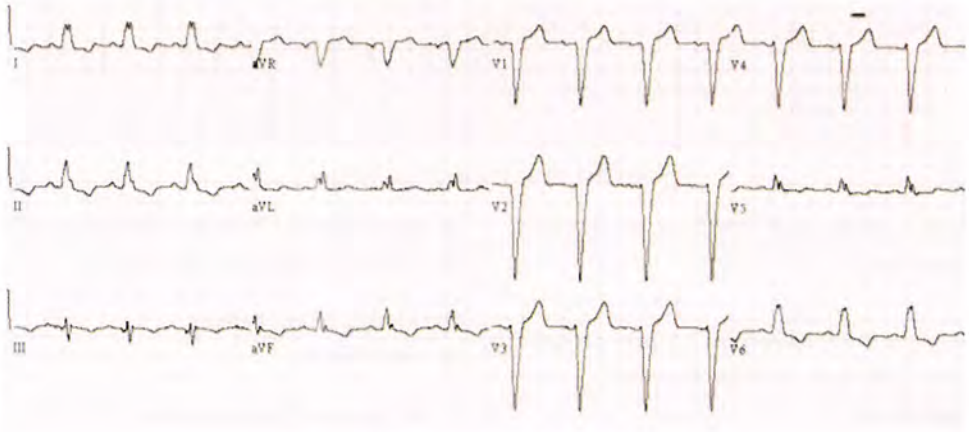
A: As follows:

- Pulse: Bradycardia (<40/min), high volume, does not increase by exercise.
- Cannon waves (large a-wave) in neck vein.
- Variable intensity of first heart sound.

Q: What is the **management**?

A: Permanent pacemaker.

ECG 10: Left Bundle Branch Block



Left bundle branch block

Q: Write down two important **abnormal findings** in this ECG.

A: As follows:

- Wide QRS complex in all leads.
- RSR' pattern in I, AVl, AVf, V5 and V6.

Q: What is your **diagnosis**?

A: Left bundle branch block.

Q: What finding might you get on **auscultation**?

A: Reverse splitting of second heart sound.

Q: Mention four **causes**.

A: As follows:

- Severe coronary artery disease.
- Acute myocardial infarction.
- Cardiomyopathy.
- Aortic valve disease (stenosis or regurgitation).

ECG 11: Right Bundle Branch Block



Right bundle branch block

Q: Write down two important **abnormal findings** in this ECG.

A: As follows:

- Wide QRS complex in all leads.
- RSR' pattern in V1, V2 and V3.

Q: What is your **diagnosis**?

A: Right bundle branch block.

Q: Mention three **causes**.

A: As follows:

- Normal variant.
- Coronary artery disease (acute myocardial infarction).
- Atrial septal defect.
- Cardiomyopathy.

ECG 12: Left Ventricular Hypertrophy

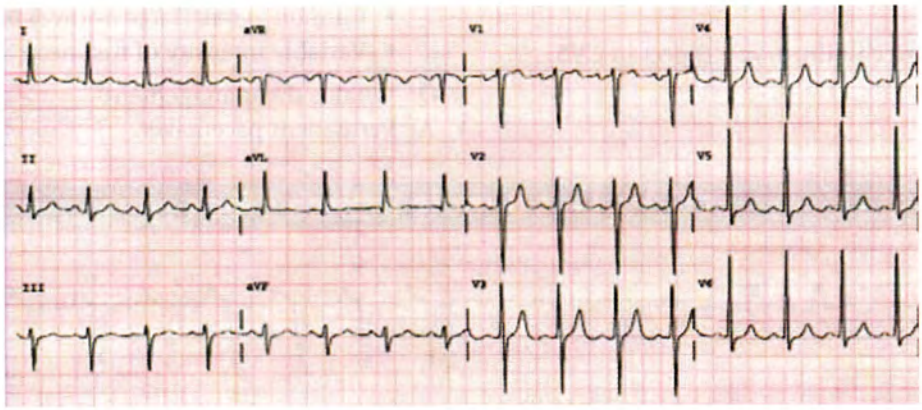


Fig. A: Left ventricular hypertrophy

Q: Write down two **abnormal findings** in the ECG shown in Figure A.

A: As follows:

- S-wave in V1 + R-wave in V6= 39 mm (criteria: S-wave in V1 + R-wave in V6> 35 mm).
- Left-axis deviation.

Q: What is your **diagnosis**?

A: Left ventricular hypertrophy.

Q: Mention one finding in examination of **precordium**.

A: Apex beat is heaving in nature.

Q: Mention one **investigation** to confirm the diagnosis.

A: Echocardiography (M-mode).

Q: Mention five **causes**.

A: As follows:

- Systemic hypertension.
- Aortic stenosis.
- Coarctation of aorta.
- Hypertrophic cardiomyopathy.
- Ventricular septal defect.

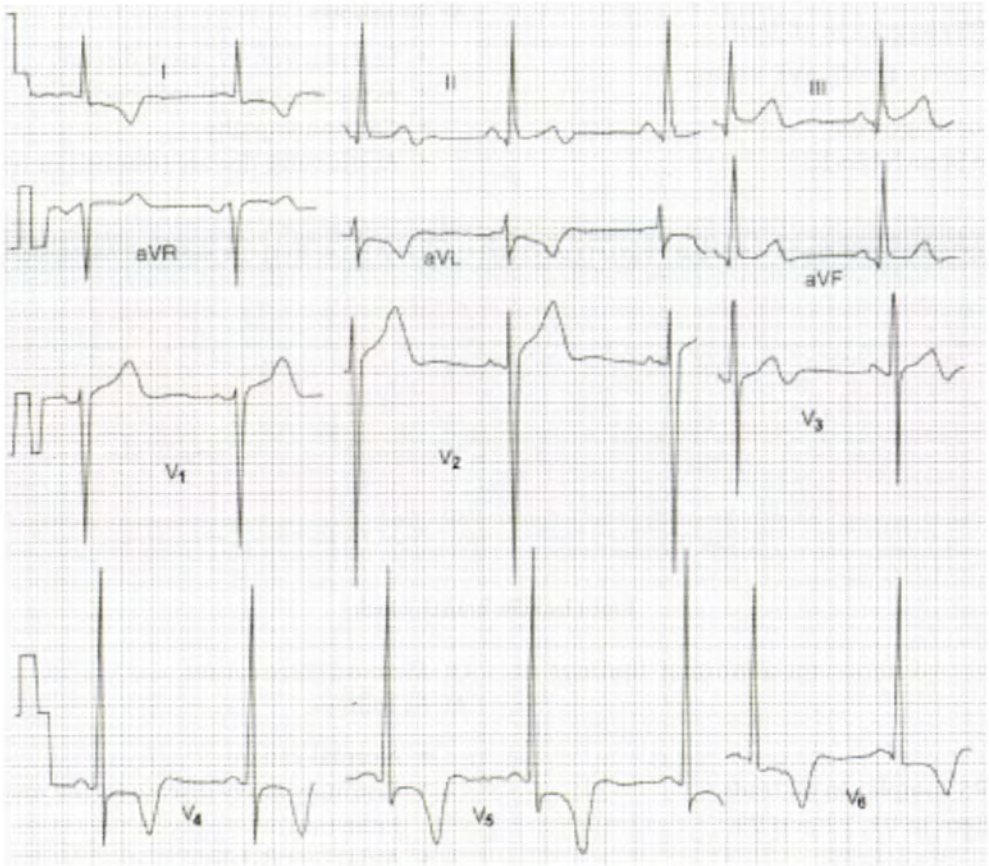


Fig. B: Left ventricular hypertrophy with strain

Q: Write down two **abnormal findings** in the ECG shown in Figure B.
A: As follows:

- S-wave in V1 + R-wave in V6= 51 mm (criteria: S-wave in V1 + R-wave in V6> 35 mm).
- ST-wave depression and T-wave inversion in L1, AVl, V4–V6.

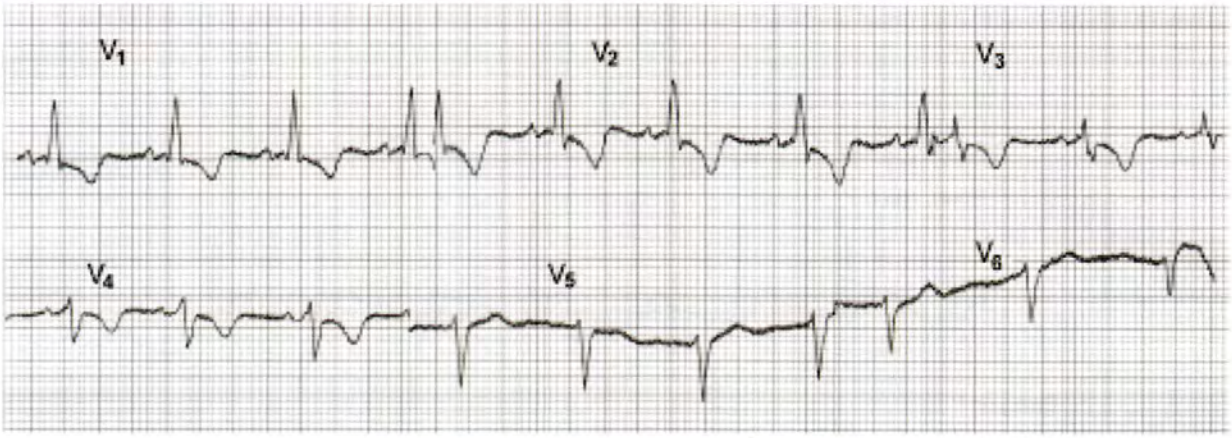
Q: What is your **diagnosis**?
A: Left ventricular hypertrophy with strain.

Q: What are the **differential** diagnoses?
A: As follows:

- Hypertrophic cardiomyopathy.
- Subendocardial myocardial infarction.

Q: Mention one **investigation** to confirm the diagnosis.
A: Echocardiography (2D or M-mode).

ECG 13: Right Ventricular Hypertrophy



Right ventricular hypertrophy with strain

Q: Write down two **abnormal findings** in this ECG.
A: As follows:

- R-wave in V1 = 10 mm (criteria: tall R-wave in V1 > 7 mm).
- ST-wave depression and T-wave inversion (in V1 and V2).

Q: What is your **diagnosis**?
A: Right ventricular hypertrophy with strain.

Q: Mention four **clinical findings**.
A: As follows:

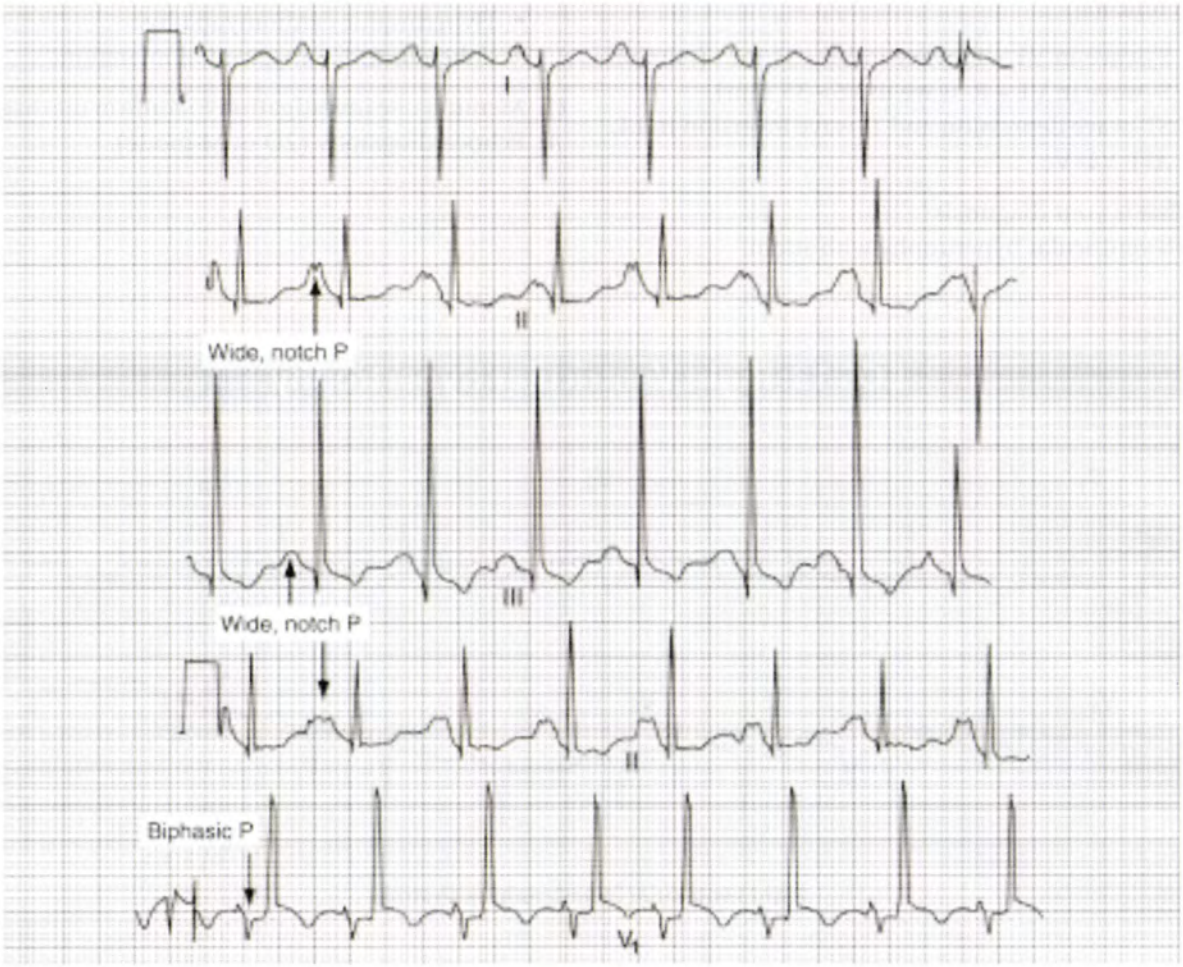
- Palpable P2.
- Left parasternal heave.
- Epigastric pulsation.
- Loud P2 on auscultation.

Q: Mention one **investigation** to confirm the diagnosis.
A: Echocardiogram (2D and M-mode).

Q: Mention five **causes**.
A: As follows:

- Chronic cor pulmonale.
- Mitral stenosis with pulmonary hypertension.
- Primary pulmonary hypertension.
- Pulmonary stenosis.
- Eisenmenger syndrome.
- Fallot tetralogy.

ECG 14: P Mitrale



P mitrale

Q: Write down three **abnormal findings** in this ECG.
A: As follows:

- P-wave is wide (> 0.12 s) in LII and III.
- P-wave is notched (or bifid) in LII (called P mitrale).
- P-wave in V1 is biphasic with prominent deep negative deflection (>1-mm depth) and small initial positive deflection.

Q: What is your **diagnosis**?
A: P mitrale.

Q: What does it **indicate**?
A: It indicates left atrial hypertrophy or enlargement.

Q: Mention two **causes** of such ECG finding.
A: As follows:

- Mitral stenosis (commonest).
- Mitral regurgitation.

ECG 15: P Pulmonale



P pulmonale

Q: What is the **abnormal finding** in this ECG?
A: P–wave is tall (>2.5 mm) in LI, II, III (P pulmonale).

Q: What is your **diagnosis**?
A: P pulmonale.

Q: What does it **indicate**?
A: It indicates right atrial hypertrophy or enlargement.

Q: Mention five **causes** of such ECG finding.
A: As follows:

- COPD with chronic cor pulmonale (commonest).
- Atrial septal defect (ASD).
- Tricuspid regurgitation or stenosis.
- Pulmonary stenosis.
- Pulmonary hypertension (due to any cause).

ECG 16: Pulsus Bigeminy



Pulsus bigeminy

Q: What is the **abnormal finding** in this ECG?
A: Every normal beat is followed by a ventricular ectopic beat.

Q: What is your **diagnosis**?
A: Ventricular bigeminy.

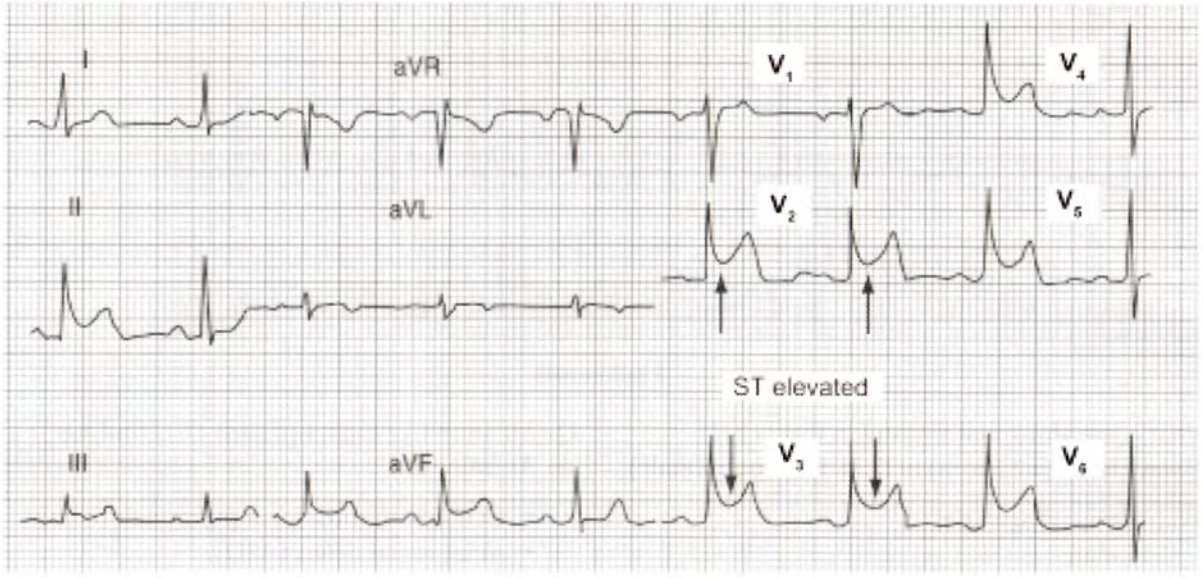
Q: Mention five **causes**.
A: As follows:

- Digoxin toxicity.
- Myocarditis.
- Cardiomyopathy.
- After acute myocardial infarction.
- Electrolyte imbalance (hypokalaemia).
- Hypoxaemia.

Q: How to **treat**?
A: As follows:

- Any offending drug should be stopped.
- Correction of electrolytes, especially hypokalaemia, hyperkalaemia and hypomagnesaemia.
- Treatment of primary cause or any organic heart disease.
- If asymptomatic: No other treatment.
- If symptomatic: β-Blocker (antiarrhythmic drugs should be avoided, may worsen the prognosis).

ECG 17: Acute Pericarditis



Acute pericarditis

Q: Mention the **abnormal finding**.
A: ST is elevated with upward concavity in LII, AVf, V2, V3, V4, V5 and V6.

Q: What is your **diagnosis**?
A: Acute pericarditis.

Q: Mention one **clinical finding**.
A: Pericardial rub.

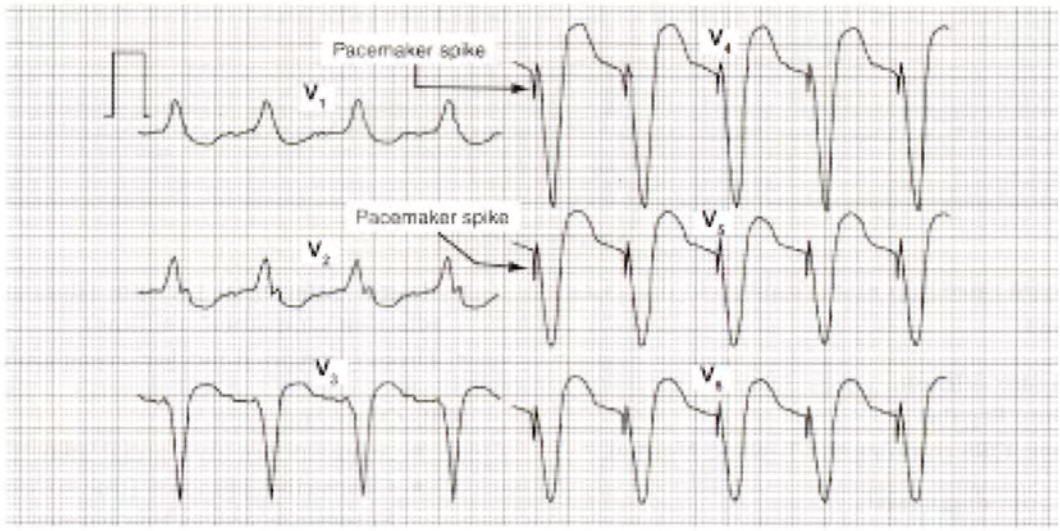
Q: Mention five **causes**.
A: As follows:

- Following acute myocardial infarction (usually in 2nd or 3rd day).
- Infective: Viral (coxsackie B, echovirus) common cause. Others are bacterial (*Staphylococcus aureus*, *Haemophilus influenzae*), tuberculous pericarditis and fungal (histoplasmosis, coccidioidomycosis).
- Acute rheumatic fever.
- Acute renal failure.
- Malignancy (from carcinoma of bronchus, breast, lymphoma, leukaemia).
- Collagen disease [systemic lupus erythematosus (SLE), scleroderma].

Q: How to **treat**?
A: As follows:

- To relieve pain—NSAID (indomethacin or ibuprofen or aspirin).
- In severe or recurrent case—corticosteroid should be given.
- If no response to steroid—azathioprine or colchicine may be given.
- If recurrence with no response to medical treatment, pericardiotomy may be done.
- Treatment of primary cause—antibiotic, if bacterial infection. Anti-Koch, if tuberculosis is suspected.

ECG 18: Pacemaker



Ventricular pacemaker

Q: Mention two **abnormal findings**.
A: As follows:

- There is a spike followed by QRS complex.
- QRS complex is wide (looks like LBBB).

Q: What is your **diagnosis**?
A: Ventricular pacemaker.

Q: Mention two **absolute indications**.
A: As follows:

- Sick sinus syndrome.
- Stokes–Adams syndrome.

ECG 19: Sinus Tachycardia



Sinus tachycardia

Q: Write down three important **findings** in this ECG.
A: As follows:

- Heart rate: 110/min.
- Rhythm: Normal.
- P-wave, QRS complex and T-wave: Normal.

Q: What is your **diagnosis**?
A: Sinus tachycardia.

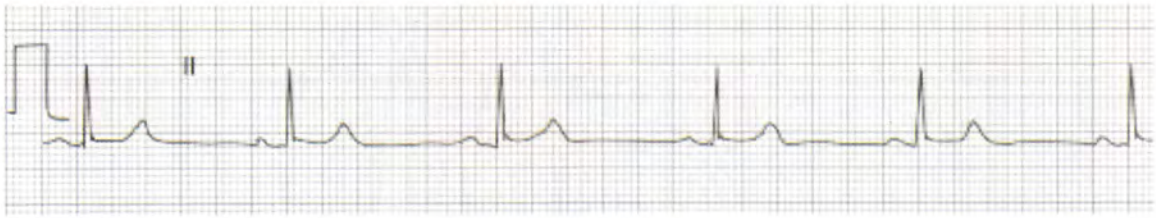
Q: Write down five important **causes**.
A: As follows:

- Physiological: Anxiety, emotion, exercise, pain, pregnancy.
- Anaemia.
- Fever.
- Thyrotoxicosis.
- Shock (except vasovagal attack in which bradycardia is present).
- Heart failure.

N.B. Other causes are:

- Chronic constrictive pericarditis.
- Acute anterior myocardial infarction (bradycardia is common in acute inferior myocardial infarction).
- Drugs (salbutamol, atropine, adrenaline, isoprenaline, ephedrine, propantheline, thyroxine).

ECG 20: Sinus Bradycardia



Sinus bradycardia

Q: Write down three important **findings** in this ECG.

A: As follows:

- Heart rate: 50/min.
- Rhythm: Regular.
- P-wave, QRS complex and T-wave: Normal.

Q: What is your **diagnosis**?

A: Sinus Bradycardia.

Q: Write down five important **causes**.

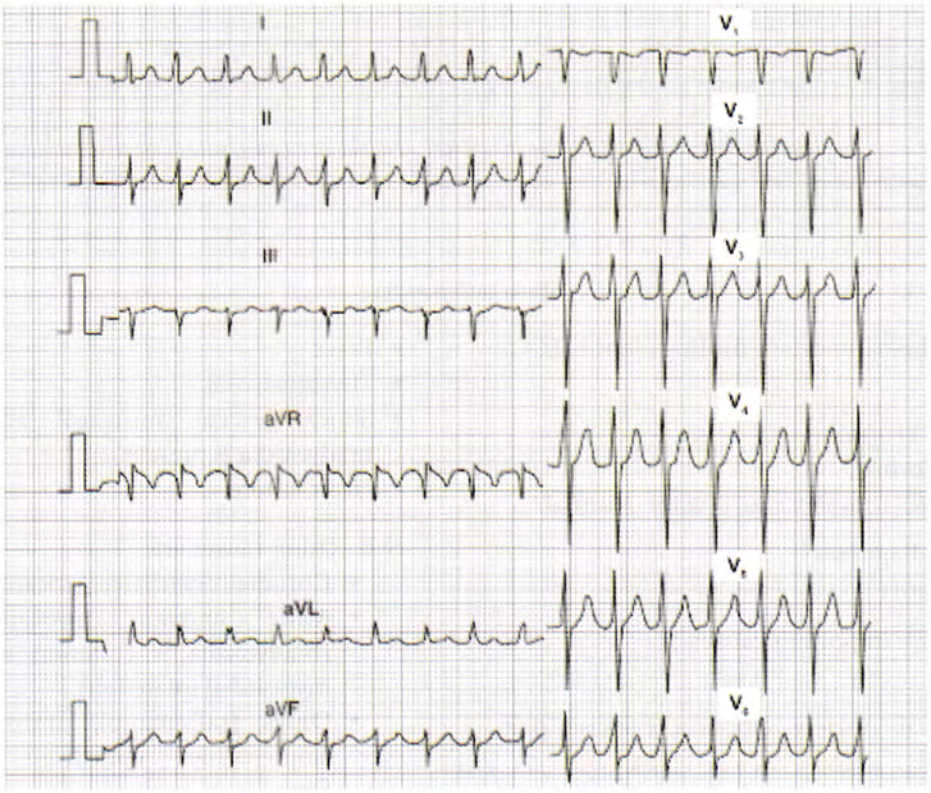
A: As follows:

- Physiological: In athletes, during sleep.
- Hypothyroidism.
- Hypothermia.
- Raised intracranial pressure (due to inhibitory effect on sympathetic outflow).
- Drugs (digoxin, β-blockers, verapamil).

N.B. Other causes are:

- Acute inferior myocardial infarction.
- Obstructive jaundice (due to deposition of bilirubin in conducting system).
- Electrolyte imbalance (hypokalaemia).
- Neurally mediated syndromes due to a reflex (Bezold-Jarisch), which causes bradycardia and reflex peripheral vasodilatation. These are—carotid sinus syndrome, neurocardiogenic (vasovagal) syncope (syndrome), which presents as syncope or presyncope.

ECG 21: Supraventricular Tachycardia



Supraventricular tachycardia

Q: Write down four important **findings** in this ECG.
A: As follows:

- Heart rate: 140/min.
- Rhythm: Regular.
- P-wave: Absent.
- QRS complex: Narrow.

Q: What is your **diagnosis**?
A: Supraventricular tachycardia.

Q: Write down five important **causes**.
A: As follows:

- Physiological: Anxiety, tea, coffee, alcohol.
- Thyrotoxicosis.
- Ischaemic heart disease.
- WPW syndrome.
- Digitalis toxicity.

Q: What is the **complication**?
A: Heart failure may occur due to reduction of stroke volume (rapid heart rate causes short diastolic filling time with low diastolic filling).

Q: How to **treat**?
A: As follows:

1. Rest and reassurance.
2. Carotid sinus massage or Valsalva manoeuvre. It acts by increasing the vagal tone.
3. If no response:
 - IV adenosine—3 mg over 2 s. If no response in 1–2 min, then 6 mg IV. If still no response in 1–2 min, then 12 mg.
 - Or IV verapamil 10 mg slowly over 5–10 min (verapamil should be avoided if QRS complex > 0.12 s or history of WPW syndrome or if the patient is on β-blocker).
4. Other drugs: β-Blocker, disopyramide or digoxin may be used.
5. If the patient is haemodynamically unstable (hypotension, pulmonary oedema), then direct current (DC) shock should be given.
6. If the attack is frequent or disabling: Prophylactic oral therapy with β-blocker, verapamil, disopyramide or digoxin may be given.
7. In WPW syndrome: Transvenous radiofrequency catheter ablation is the treatment of choice.
8. If there is no response: Antitachycardial pacing is done (overdrive atrial pacing).

ECG 22: Ventricular Premature Beat



Ventricular premature beat

Q: Write down three important **findings** in this ECG.
A: There are two ventricular premature beats with the following characteristics:

- P: Absent.
- QRS complex: Wide >0.12 s (3 small squares).
- T: Opposite to major deflection.

Q: What is your **diagnosis**?
A: Ventricular premature (ectopic) beats.

Q: Write down five important **causes**.
A: As follows:

- Normally in young adults, also in anxiety, excess caffeine, alcohol.
- Acute myocardial infarction.
- Myocarditis.
- Cardiomyopathy.
- Electrolyte imbalance (especially hypokalaemia).
- Digoxin toxicity.
- Mitral valve prolapse.

Q: What are the **types**?
A: As follows:

- *Unifocal:* Similar configuration of ectopics in all leads, originates from a single ectopic ventricular focus.
- *Multifocal:* Variable configuration of ectopics in same lead, ectopics originate from different foci of ventricle.
- *Interpolated ventricular ectopics:* It means when ventricular ectopics occur between two normal sinus beat without compensatory pause.

Other Types

- *Couplet:* Two ventricular ectopics in a row, multifocal.

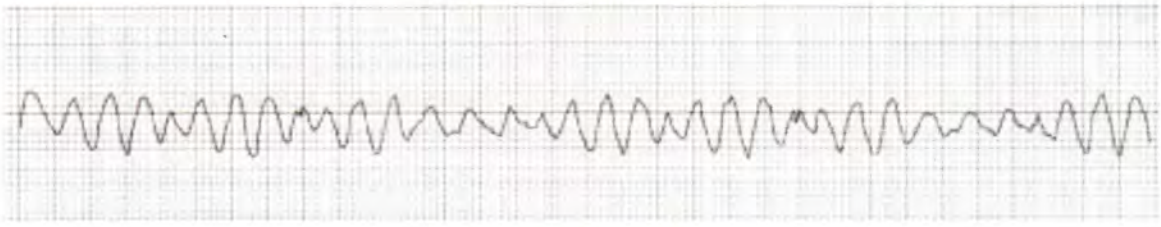
- *Triplet:* Three ventricular ectopics in a row (runs of ectopic, three or more ventricular ectopics in a row, may be taken as ventricular tachycardia).
- *Ventricular bigeminy:* Every one normal beat followed by ventricular ectopic.
- *Ventricular trigeminy:* Every two normal beats followed by ventricular ectopic.
- *Ventricular quadrigeminy:* Every three normal beats followed by ventricular ectopic.
- *Grouped ventricular ectopics:* Two to five consecutive ventricular ectopics.

Q: How to **treat**?

A: As follows:

- In the absence of any heart disease and in asymptomatic case: No treatment is necessary. β-Blocker may be used.
- With organic heart disease: Treatment of primary cause.

ECG 23: Ventricular Fibrillation



Ventricular fibrillation

Q: What is the **finding** in this ECG.

A: QRS complex: Chaotic, wide, bizarre, irregular.

Q: What is your **diagnosis**?

A: Ventricular fibrillation.

Q: Write down five important **causes**.

A: As follows:

- Acute myocardial infarction.
- Electrolyte imbalance (hypokalaemia, hypomagnesaemia).
- Electrocution.
- Drowning.
- Drug overdose (digitalis, adrenaline, isoprenaline).

Q: Mention six clinical **signs** in this patient.

A: As follows:

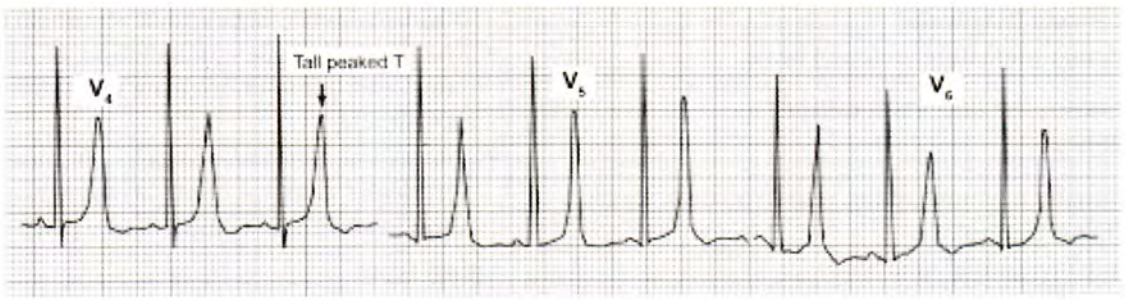
- Pulse: Absent.
- BP: Not recordable.
- Respiration: Ceases or absent.
- Patient: Unconscious.
- Pupil: Dilated, less or no reaction to light.
- Heart sounds: Absent.

Q: How to **treat**?

A: As follows:

- Immediate defibrillation: 200 Joules. If no response, another shock with 200 Joules is given. If still no response, another shock with 360 Joules is given.
- If three shocks unsuccessful: Adrenaline is given IV, followed by cardiopulmonary resuscitation.
- If defibrillator is not available: Cardiopulmonary resuscitation should be given.
- The patient who survives from ventricular fibrillation (VF) in the absence of identifiable cause is at high risk of sudden death. This case is treated with implantable cardioverter defibrillator.

ECG 24: Hyperkalaemia



Hyperkalaemia

Q: Write down two important **findings** in this ECG.
A: As follows:

- T–wave: Tall, peaked and tented.
- P–wave: Wide and small.

N.B. Other probable findings are (not seen in this ECG):

- P–R interval: Prolonged.
- QRS complex: Wide, slurred and bizarre.

Q: What is your **diagnosis**?
A: Hyperkalaemia.

Q: Write down four important **causes**.
A: As follows:

1. High potassium intake.
2. Renal diseases:
 - Acute and chronic renal failure.
 - Impaired tubular secretion of K+ (renal lupus, amyloidosis, transplanted kidney).
3. Endocrine diseases:
 - Addison disease.
 - Diabetic ketoacidosis.
 - Primary hypoaldosteronism.
4. Drugs: Potassium sparing diuretics (spironolactone, amiloride, triamterine), ACE inhibitor, NSAID, cyclosporine.

Q: Write four clinical **features**.
A: As follows:

- Muscular weakness; it may be severe causing flaccid paralysis, loss of tendon jerk.
- Paralytic ileus (abdomen may be distended).
- Tingling around the lip or finger.
- Sudden death due to cardiac arrest or arrhythmia.

Q: How to **treat**?
A: As follows:

- Withdrawal of potassium, potassium-containing food and offending drug.
- Injection 10% calcium gluconate 10–20 cc IV slowly over 10 min.
- Injection 50 ml of 50% glucose IV + Inj. insulin 10 units.
- Correction of acidosis: By IV sodibicarb (1.26%), 500 ml 6–8 hourly (until serum HCO_3 is normal).
- Treatment of primary causes.
- In some cases, exchange resins (calcium resonium 15–30 gm orally).
- If all fail: Haemodialysis or peritoneal dialysis.

CHAPTER 16

PICTURES

"Diagnosis is not the end, but the beginning of practice"

– Martin H. Fischer

Picture 01: Infected Scabies



Q: Write down the **finding** shown in this picture.

A: Multiple vesicular and pustular lesions in interdigital and dorsal surface of both hands.

Q: What is your **diagnosis**?

A: Infected scabies.

Q: What is the causative **organism**?

A: *Sarcoptes scabiei*.

Q: What are the common **sites**?

A: As follows:

- Interdigital space.
- Anticubital fossa.
- Axilla.
- Nipple.
- Umbilicus.
- Scrotum.

Q: What are the **differential** diagnoses?

A: As follows:

- Popular urticarial.
- Atopic dermatitis.
- Dermatitis herpetiformis.
- Pediculosis corporis.

Q: Write down two important **complications** of this clinical condition.

A: Secondary bacterial infection, poststreptococcal glomerulonephritis.

Q: Write down the **treatment**.

A: As follows:

1. General measures: Control of infection by antibiotics; for itching–antihistamine, washing of cloths and bed sheet, simultaneous treatment of other family members.
2. Specific treatment:
 - Local: 5% permethrin cream. Other drugs are 1% γ-benzene hexachloride, 25% benzyl benzoate, 10% precipitated sulfur in white petroleum.
 - Systemic: Ivermectin orally when local treatment fails.

Picture 02: Purpura



Q: What are the **findings** seen in the photograph?
A: Multiple purpuric spot of variable size and shape in both lower limbs.

Q: Mention six **differential** diagnoses.
A: As follows:

- Drug rash.
- Idiopathic thrombocytopenic purpura (ITP).
- Henoch–Schonlein purpura.
- Dengue haemorrhagic fever.
- Aplastic anaemia.
- Meningococcal septicaemia.

Q: Mention six important **investigations** for this patient.
A: As follows:

- Complete blood count (CBC) with peripheral blood film (PBF).
- Antidengue antibody.
- Blood for culture and sensitivity (C/S).
- Coagulation profile: Prothrombin time, activated partial thromboplastin time (APTT).
- Screening for disseminated intravascular coagulation (DIC): Fibrin degradation products (FDP), D-dimer.
- Bone marrow study.

Picture 03: Rheumatoid Arthritis



Q: What are the **abnormalities** in this photograph?
A: As follows:

- Swan-neck deformity of fingers.
- Z-deformity of thumb.
- Ulnar deviation of hands.
- Flexion deformity of metacarpophalangeal joints.

Q: What is the **diagnosis**?
A: Rheumatiod arthritis.

Q: Mention five important **investigations**.
A: As follows:

- CBC, erythrocyte sedimentation rate (ESR).
- C-reactive protein (CRP).

- Rheumatoid arthritis (RA) and Rose–Waaler (RW) tests.
- Anti-cyclic citrullinated peptide (anti-CCP) antibody.
- X-ray of both hands.

Q: Mention the modalities of **treatment**.

A: As follows:

1. To relieve pain: NSAID.
2. Suppression of activity and progression of disease: DMRD.
3. Physiotherapy.
4. Orthopaedic measures.

Picture 04: Arthritis Mutilans



Q: What are the **findings**?

A: Complete disorganization and deformity involving all the joints of both hands.

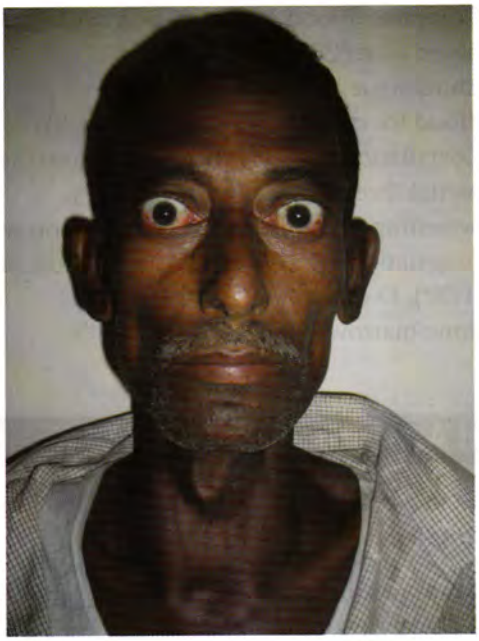
Q: What is the likely **diagnosis**?

A: Arthritis mutilans in rheumatoid arthritis.

Q: What specific **measures** can be done in such a case?

A: Orthopaedic measures such as reconstructive surgery along with treatment of rheumatoid arthritis.

Picture 05: Graves Disease



Q: Write down four important **findings** in this picture.

A: As follows:

- Bilateral exophthalmos.
- Diffuse goitre.
- Anxious look.
- Wasting.

Q: What is your **diagnosis**?

A: Graves disease.

Q: What **other finding** you should look for in this case?

A: Dermopathy.

Q: Mention three important **questions** you will ask the patient.

A: As follows:

- Preference to hot or cold.
- Increased appetite and weight loss.
- Excessive sweating.

Q: Write down three important **clinical findings**.

A: As follows:

- Palm: Warm and sweaty.
- Tremor of outstretched hand.
- Tachycardia.

Q: Write down the most important **investigation** to diagnose the case.

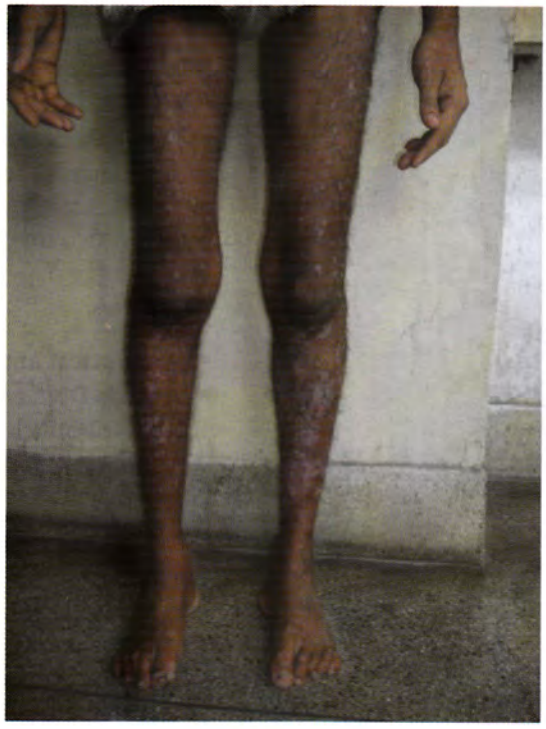
A: As follows:

- Free triiodothyronine (FT_3), free thyroxine (FT_4), thyroid stimulating hormone (TSH).
- Radioiodine uptake test.
- Thyroid scanning.
- Ultrasonogram of neck.
- TSH receptor antibody.

Q: What is the **natural history** of this disease?

A: The patient may be hyperthyroid, followed by euthyroid and then followed by hypothyroid.

Picture 06: Psoriasis



Picture A

Q: Write down the important **findings** in Picture A.
A: Multiple, well-circumscribed erythematous plaques with silvery white scales on both lower limbs.

Q: What is your **diagnosis**?
A: Psoriasis.



Picture B

Q: Write down the important **findings** in Picture B.
A: Multiple, well-circumscribed erythematous plaques with silvery white scales on the back.

Q: What is your **diagnosis**?
A: Psoriasis.

Q: What are the **differential** diagnoses?
A: As follows:

- Dermatomyositis.
- Lichen planus.
- Seborrhoeic dermatitis.
- Secondary syphilis.

Q: Mention two important **physical signs** that should be seen in this patient.
A: Auspitz sign and Koebner phenomenon.

Q: Mention one **investigation** to confirm your diagnosis.
A: Skin biopsy.

Q: How to **treat**?
A: As follows:

1. General measures: Explanation and reassurance, avoid trauma.
2. Specific therapy:
 - Local therapy: Crude tar 3–5%, dithranol, calcipotriol, ultraviolet radiation (UVR).
 - Systemic therapy: PUVA (psoralen plus UV ray), retinoid, methotrexate (MTX).
3. Other therapy: anti-TNF–α (infliximab, etanercept).

Picture 07: Systemic Lupus Erythematosus



Q: Write down the important **findings** in this picture.
A: Multiple skin rashes on the face along the butterfly distribution.

Q: What is your **diagnosis**?
A: Systemic lupus erythematosus (SLE).

Q: Mention four **differential** diagnoses.
A: As follows:

- Dermatomyositis.
- Drug rash.
- Post-kala-azar dermal leishmaniasis (PKDL).
- Lepromatous leprosy.

Q: Mention two **investigations** to confirm your diagnosis.
A: As follows:

- Antinuclear antibody (ANA).
- Anti-ds-DNA (Anti-double-stranded deoxyribonucleic acid).

Q: Name five **drugs** that may cause this disease.
A: As follows:

- Hydralazine.
- Procainamide.
- Anticonvulsant: Carbamazine, phenytoin.
- Penicillamine.
- Oral contraceptive pill.
- Isoniazid (INH).

Picture 08: Erythema Multiforme



Picture A



Picture B

Q: Write down the important **findings** in these pictures.
A: Multiple erythematous vesicular lesions on both forearms and erythematous lesions involving both palms.

Q: What is your **diagnosis**?
A: Erythema multiforme.

Q: What is the **pathognomonic lesion** in this disease?
A: Target lesion.

Q: What are the **differential** diagnoses?
A: As follows:

- Drug reaction.
- SLE.
- Dermatitis herpetiformis.
- Dermatomyositis.

Q: Mention two causes.
A: As follows:

- Infection: Herpes simplex type 1, *Mycoplasma pneumoniae*.
- Drugs: Sulfonamide, carbamazepine, thioacetazone.

Q: What investigations should be done?
A: As follows:

- CBC, ESR.
- Antibody to herpes simplex virus and *Mycoplasma pneumoniae*.
- Chest X-ray.

Picture 09: Leprosy



Q: Write down the important findings in this picture.
A: As follows:

- Multiple erythematous nodules of variable size and shape on forehead, ear and face.
- Multiple pigmented and depigmented areas over the same area.

Q: What is your diagnosis?
A: Lepromatous leprosy.

Q: What is the causative organism?
A: *Mycobacterium leprae*.

Q: Mention four differential diagnoses.
A: As follows:

- Post-kala-azar dermal leishmaniasis (PKDL).
- Sarcoidosis.
- Drug rash.
- Dermatomyositis.

Q: What investigations should be done to confirm the diagnosis?
A: Skin slit smear for acid fast bacilli (AFB) staining.

Q: What drugs are used to treat the case?
A: As follows:

- Dapsone.
- Rifampicin.
- Clofazimine.

Picture 10: Stevens–Johnson Syndrome



Picture A

Q: Write down the important findings in Picture A.
A: Multiple erythematous lesions and ulcerations involving skin and mucous membrane of face, lips and oral cavity.

Q: What is your diagnosis?
A: Stevens–Johnson syndrome.



Picture B

Q: Write down the important **findings** in Picture B.

A: As follows:

- Desquamation and ulceration of skin of scrotum.
- Multiple, sharply demarcated pigmented lesions over lower abdomen and upper thighs.

Q: What is your **diagnosis**?

A: Stevens–Johnson syndrome.

Q: Mention three **causes**.

A: As follows:

- Drug reaction: Sulfonamide, carbamazepine, thiacetazone.
- Infection by herpes simplex virus, *Mycoplasma pneumoniae*.
- Idiopathic.

Picture 11: Ring Worm



Q: Write down the important **findings** in this picture.

A: Multiple circular lesions on both antecubital fossa, showing central healing with peripherally active lesion.

Q: What is your **diagnosis**?

A: Ring worm infection (*Tinea corporis*).

Q: How to **confirm**?

A: Microscopic examination of skin scrapping in KOH preparation.

Q: What are the causative **organisms**?

A: As follows:

- Trichophyton.
- Epidermophyton.
- Mycosporum.

Q: How to **treat**?

A: As follows:

- Maintain hygiene.
- Local antifungal like miconazole.
- Systemic antifungal like fluconazole.

Picture 12: Subconjuctival Haemorrhage



Q: Write down the important **findings** in this picture.

A: Subconjuctival haemorrhage in both eyes.

Q: Mention three **causes**?

A: As follows:

- Trauma.
- Dengue fever.
- Bleeding disorder.

Q: How to **treat**?

A: As follows:

- Local: Antibiotic eye drop, analgesics for pain.
- Treatment of the cause.

Picture 13: Bell Palsy



Picture A

Q: Write down the important **findings** in Picture A.

A: As follows:

- Difficulty in closing the right eye (mention if Bell phenomenon is also seen).
- Mouth is deviated to the left on showing the teeth.
- No wrinkling of the forehead on right side.
- Facial asymmetry.
- Nasolabial fold less prominent on right side.

Q: What is your **diagnosis**?

A: Right-sided Bell palsy.



Picture B

Q: Write down the important **findings** in Picture B.

A: As follows:

- Bell's phenomenon on closing the right eye.
- Nasolabial fold less prominent on right side.

Q: What is your **diagnosis**?

A: Right-sided Bell palsy.

Q: What are the **causes** if it was bilateral?

A: As follows:

- Guillain–Barre syndrome (GBS).
- Sarcoidosis.
- Lyme disease.

Q: How to treat?

A: As follows:

- Prednisolone 40–60 mg daily plus acyclovir for 7 days.
- Artificial tear.
- Physiotherapy.

Picture 14: Ramsay Hunt Syndrome



Q: What is the **finding** in this picture?

A: Vesicular rash on external ear with pus in external auditory meatus.

Q: This patient also has right-sided facial palsy. What is the **diagnosis**?

A: Ramsay Hunt syndrome.

Q: What is the **cause**?

A: Varicella-zoster virus.

Picture 15: Goitrous Myxoedema



Q: What are the abnormal **findings** in this picture?
A: As follows:

- Diffuse goitre.
- Puffy face.

Q: What is the likely **diagnosis**?
A: Goitrous myxoedema.

Q: Mention two **causes**.
A: As follows:

- Hashimoto thyroiditis.
- Iodine-deficiency goitre.

Q: Write three **clinical features**.
A: As follows:

- Intolerance to cold.
- Weight gain.
- Increased sleepiness.

Q: Write one important bedside physical **sign**.
A: Slow relaxation of ankle jerk.

Q: If the patient complains of **tingling and numbness** of fingers, what is the likely diagnosis?
A: Carpal tunnel syndrome.

Q: Mention three **investigations** to confirm your diagnosis.
A: As follows:

- FT_3, FT_4, TSH.
- Antithyroglobulin and antiperoxidase antibody.
- Ultrasonogram of neck.

Q: How to **treat**?
A: Lifelong thyroxine therapy.

Picture 16: Gonorrhoea



Q: Write down the important **finding** in this picture.
A: Purulent urethral discharge.

Q: What is your **diagnosis**?
A: Gonorrhoea.

Q: What **investigations** should be done?
A: Urethral swab for Gram stain and C/S.

Q: How to **treat**?
A: Antibiotic like ceftriaxone, ciprofloxacin, etc.

Picture 17: Hirsutism



Picture A

Q: What is the **finding** in Picture A?
A: Increased facial hair in an elderly female patient.

Q: What is the **diagnosis**?
A: Hirsutism.

Q: Mention three **causes**?
A: As follows:

- Androgen-secreting ovarian tumour.
- Adrenal carcinoma.
- Idiopathic.



Picture B

Q: Mention three **findings** in Picture B.
A: As follows:

- Increased facial hair in a young female patient.
- Puffy face with flushing.
- Facial acne.

Q: What is the **likely diagnosis** in this patient?
A: Cushing syndrome.

Q: Mention three **differential** diagnosis:
A: As follows:

- PCOS.
- Androgen-secreting ovarian tumour.
- Late-onset congenital adrenal hyperplasia.

Picture 18: Osteoarthrosis



Q: What are the **findings** in this picture?
A: Nodular swelling on the distal interphalangeal joint of right little and ring fingers.

Q: What is the likely **diagnosis**?
A: Osteoarthrosis.

Q: What is the **lesion** called?
A: Heberden node.

Picture 19: Peripheral Vascular Disease



Q: What is the **finding** in this picture?

A: Blackening and necrosis of index fingers of both hands and middle and little fingers of left hand.

Q: What is the **diagnosis**?

A: Peripheral vascular disease, most likely Buerger disease.

Q: Mention three **differential diagnoses**.

A: As follows:

- Atherosclerosis.
- Raynaud disease.
- Systemic sclerosis.

Picture 20: Hypopituitarism



Q: What are the findings in this picture of a 45-year-old man?

A: As follows:

- Short stature.
- Bilateral gynaecomastia.

Q: What is the likely diagnosis?

A: Hypopituitarism.

Q: Mention one investigation.

A: Magnetic resonance imaging (MRI) of the pituitary fossa.

Picture 21: Herpes Zoster



Picture A

Q: What is the **finding** in Picture A?
A: Multiple vesicular lesions over left shoulder, left upper chest and upper part of left arm along left C4 dermatome.

Q: What is the **diagnosis**?
A: Herpes zoster.

Q: How to **treat**?
A: Acyclovir and local skin care (such as antiseptic cream, regular cleaning)

Q: Mention one complication.
A: Post herpetic neuralgia.



Picture B

Q: What is the **finding** in Picture B?
A: Ulcerated lesions over right-half of forehead, around the right eye and over the right maxillary region.

Q: What is the **diagnosis**?
A: Herpes zoster ophthalmicus.

Q: What is the causative **organism**?
A: Varicella-zoster virus.

Q: How to **treat**?
A: As follows:

- Acyclovir.
- Care of the eye.

Picture 22: Obstructive Jaundice



Q: Write two **findings** in this picture?
A: As follows:

- Deep jaundice.
- Cachexia.

Q: What is the likely **diagnosis**?
A: Obstructive jaundice, most likely due to carcinoma of head of pancreas.

Q: Mention three **investigations**.
A: As follows:

- Liver function tests: Serum bilirubin, alanine aminotranferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase, prothrombin time.
- Ultrasonogram of hepatobiliary system and pancreas.
- CT scan of abdomen.

Picture 23: Wegener Granulomatosis



Q: What are the **findings**?
A: Swelling on the forehead, left upper eyelid and nasal bridge.

Q: This patient presented with recurrent rhinitis with cough. What is the likely **diagnosis**?
A: Wegener granulomatosis.

Q: Mention three **investigations**.
A: As follows:

- X-ray of chest PA view.
- Cytoplasmic antineutrophil cytoplasmic antibodies (c-ANCA).
- Biopsy from nasal crust or affected part.

Q: What are the **differential** diagnoses?
A: As follows:

- Sarcoidosis.
- Lymphoma.
- Tuberculosis.
- Midline granuloma (idiopathic).
- Fungal: Histoplasmosis.
- Lymphomatoid granulomatosis.
- Rhinoscleroma.

Picture 24: Xanthelasma



Q: What is the **finding** in this picture?
A: Xanthelasma.

Q: What does it **indicate**?
A: Dyslipidaemia.

Q: What **investigation** should be done?
A: Fasting lipid profile.

Q: Mention three **causes**.
A: As follows:

- Primary biliary cirrhosis.
- Nephrotic syndrome.
- Familial hypercholesterolaemia.

Picture 25: Baker Cyst



Q: What is the likely **diagnosis**?
A: Baker cyst.

Q: Mention three **causes**.
A: As follows:

- Rheumatoid arthritis.
- Osteoarthrosis.
- Congenital.

Q: Mention one **complication**.
A: Rupture of Baker cyst.

Q: What is the **finding** in this picture?
A: Swelling on the back of right knee.

Q: Mention one **investigation**.
A: Ultrasonogram of the knee joint.

Picture 26: Pectus Carinatum



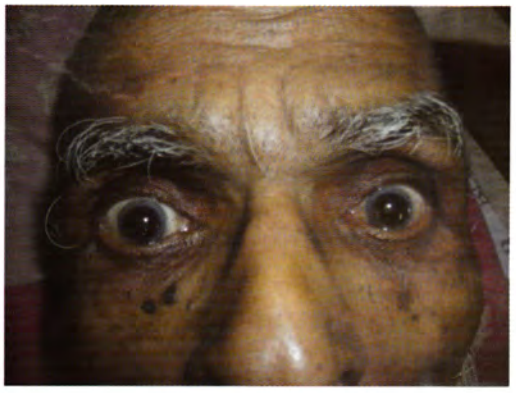
Q: What are the **findings** in this picture?
A: As follows:

- Pectus carinatum (pigeon chest).
- Kyphosis.

Q: What are the **causes**?
A: As follows:

- Congenital.
- Ricket.
- Marfan syndrome.
- Homocystinuria.
- Repeated respiratory infection in childhood.
- Bronchial asthma since childhood.
- Osteogenesis imperfecta.

Picture 27: Corneal Arcus



Q: Write down the abnormal **finding** in the eyes of this 75-year-old patient.
A: Whitish opaque ring around the corneal margin.

Q: What is it **called**?
A: Corneal arcus.

Q: Mention two **causes**.
A: As follows:

- Arcus senilis.
- Dyslipidaemia.

Picture 28: Acromegaly



Q: What is the abnormal **finding**? What is it **called**?
A: Protrusion of the lower jaw. It is called prognathism.

Q: What is the likely **diagnosis**?
A: Acromegaly.

Q: Mention four other **clinical findings** in this patient.
A: As follows:

- Enlarged skull, body and limbs.
- Hands are large, spade like.
- Thick skin with skin tag.
- Bitemporal hemianopia.

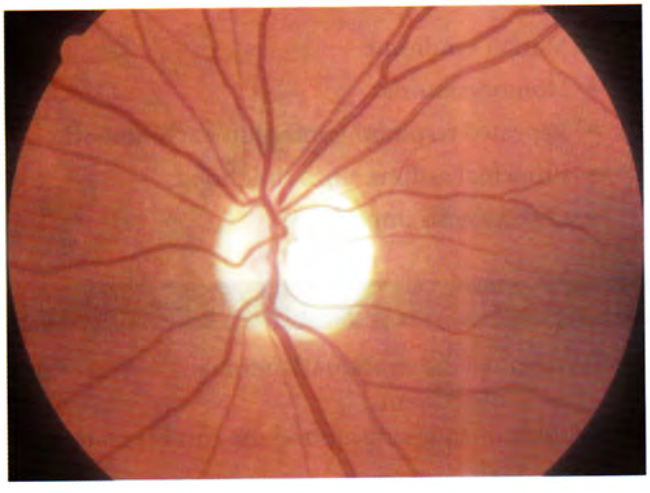
Q: What **investigations** should be done to confirm your diagnosis?
A: As follows:

- X-ray of skull, hands.
- MRI of brain.
- Growth hormone measurement with simultaneous oral glucose tolerance test (OGTT).
- Insulin-like growth factor-1 (IGF-1).

Q: What are the modalities of **treatment**?
A: As follows:

- Medical treatment: Octreotide.
- Surgical: Transphenoidal removal of pituitary tumour.
- Radiotherapy.

Picture 29: Primary Optic Atrophy



Q: What are the **findings**?
A: As follows:

- The disc is pale with clear margin.
- There is reduction of number of capillaries in the disc.

Q: What is the **diagnosis**?
A: Primary optic atrophy.

Q: What is the **mechanism**?
A: Degeneration of optic nerve fibers.

Q: Mention four **causes**.
A: As follows:

- Intracranial-space-occupying lesion.
- Secondary to optic neuritis.
- Glaucoma.
- Optic nerve compression by tumour or aneurysm.

Picture 30: Papilloedema



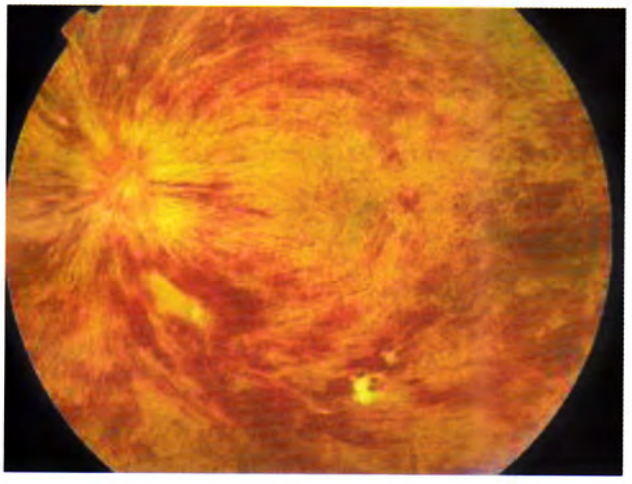
Q: What is the **finding** in this picture?
A: There is blurring of the disc margin with fullness of the optic disc.

Q: What is the **diagnosis**?
A: Papilloedema.

Q: Mention two **causes**?
A: As follows:

- Raised intracranial pressure due to space-occupying lesion (e.g. tumour, abscess, haematoma).
- Benign intracranial hypertension.

Picture 31: Central Retinal Vein Occlusion



Q: What are the **findings**?
A: As follows:

- Multiple scattered haemorrhages over the whole retina giving a stormy sunset appearance.
- Veins are dilated and tortuous.
- Few soft exudates and papilloedema are present.

Q: What is the **diagnosis**?
A: Central retinal vein occlusion.

Q: Mention five **causes**.
A: As follows:

- Hypertension.
- Atherosclerosis.
- Diabetes mellitus.
- Hyperviscosity syndrome.
- Hyperlipidaemia.

Q: Mention three serious **complications**.
A: As follows:

- Glaucoma (rubeotic).
- Optic atrophy.
- Permanent loss of vision.

Q: What **investigations** should be done?
A: As follows:

- Complete blood count (CBC).
- Blood sugar.
- Plasma viscosity.
- Plasma protein electrophoresis.
- Lipid profile.
- Bone marrow (to exclude multiple myeloma).

CHAPTER 17

INSTRUMENTS

"When you no longer know what headache, heartache, or stomachache means without cistern punctures, electrocardiograms and six x-ray plates, you are slipping"

– Martin H. Fischer

Instrument 01: Bone Marrow Aspiration Needle



Q: What is this **instrument**?

A: Bone marrow aspiration needle (also called sternal puncture needle).

Q: What are the **parts**?

A: Three parts:

- Trocar.
- Cannula.
- Adjustable guard.

Q: Mention the **sites** of use.

A: As follows:

- Manubrium sternae or body of sternum.
- Posterior superior iliac crest.
- Other sites: Upper part of the medial surface of tibia just below the tibial tuberosity in children. Rarely, spinous process of lumbar vertebrae.

Q: How can you **confirm** that the needle has **reached** the cavity?

A: When the needle is in the bone marrow cavity, there is sudden loss of resistance and marrow material is seen at the tip of the trochar.

Q: What are the **indications** of bone marrow study?

A: As follows:

- Aplastic anaemia.
- Megaloblastic anaemia.
- Macrocytic anaemia due to any cause.
- Multiple myeloma.
- Leukaemia.
- Myelofibrosis.
- Pancytopaenia due to any cause.
- Idiopathic thrombocytopaenic purpura (ITP).
- Kala-azar to see Leishman–Donovan (LD) bodies.

Q: What are the **contraindications**?

A: As follows:

- Local infection or sepsis.
- Bleeding disorder like haemophilia.
- Platelet count <40,000/cmm.

Q: What are causes of **dry or blood tap**?

A: As follows:

- Faulty technique.
- Myelosclerosis or myelofibrosis.
- Marrow hypoplasia.
- Sometimes in marrow hyperplasia or leukaemia, if the marrow is heavily packed with cells.
- Tumour infiltration, e.g. lymphoma, secondary malignancy.

Q: What are the **complications**?

A: As follows:

- Suction pain.
- Vasovagal attack due to fear or pain.
- Bleeding and localized haematoma.
- Injury to underlying structure due to over penetration.
- Infection, e.g. osteomyelitis.

Q: What is **trephine** biopsy?

A: Trephine biopsy shows histological section that contains bony trabeculae, haemopoietic tissue, fat cells and blood vessels.

Q: What are the **indications** of trephine biopsy?
A: As follows:

- Dry or blood tap.
- In aplastic anaemia: For better assessment of cellularity.
- Myelofibrosis or myelosclerosis.
- If bone marrow aspiration fails to establish a diagnosis.
- Diagnosis and staging of lymphoma.
- Secondary deposit.

Instrument 02: Lumbar Puncture Needle



Q: What is this **instrument**?
A: Lumbar puncture needle.

Q: What are its **parts**?
A: As follows:

- Cannula with cap.
- Trocar.

Q: What are the **uses**?
A: As follows:

1. Diagnostic:
 - Meningitis.
 - Encephalitis.
 - Subarachnoid haemorrhage.
 - Guillain–Barre syndrome.
 - Multiple sclerosis.
2. Therapeutic:
 - Intrathecal methotrexate in acute lymphoblastic leukaemia (ALL).
 - Spinal anaesthesia.
 - Removal of CSF in benign intracranial hypertension.

Q: Mention the anatomical **sites** of using this instrument. Why this site is chosen?
A: In the space between L3 and L4 or L4 and L5. This site is chosen because the spinal cord is absent at this space. So, there is no chance of injury.

N.B. The line between the highest points of both iliac crests runs through the spinous process of the 4th lumbar vertebra.

Q: What are the **contraindications**?
A: As follows:

- Raised intracranial pressure (clinically detected if there is papilloedema).
- Localized infection.
- Bleeding disorder (e.g. haemophilia, Christmas disease, etc.).

Q: What **clinical examination** would you do before lumbar puncture? Why?
A: Ophthalmoscopy to see papilloedema, which indicates raised intracranial pressure. If lumbar puncture is done in such case, there may be herniation of cerebellar tonsil through foramen magnum, and may compress the vital centre in medulla oblongata and cause sudden death.

Q: What are the **complications**?
A: As follows:

- Post lumbar puncture headache.
- Infection (causing meningitis, arachnoiditis).
- Bleeding.
- Herniation of cerebellar tonsil.
- Persistent cerebrospinal fluid (CSF) leaking.
- Injury to local structures like intervertebral disc, vessels, nerves, etc.

Q: Why **post lumbar puncture headache**? How to **manage**?
A: Headache usually occurs if lumbar puncture (LP) is done in normal intracranial tension. It is due to low intracranial tension due to withdrawal of CSF, which causes traction on the meningeal blood vessel resulting in headache.

Treatment is as follows:

- Increased fluid intake.
- The patient should lie flat for 8–24 h.
- Foot-end should be raised and pillow should be removed.
- Analgesic.

Q: **How much** CSF is drawn during LP?
A: For diagnostic purpose, 5–8 ml and for therapeutic purpose, 10–20 ml is drawn.

Q: What are the causes of **dry tap**?
A: As follows:

- Faulty technique.
- Spinal subarachnoid block (e.g. due to meningioma, neurofibroma, epidural abscess, etc.).

Q: What should be **seen in CSF**?
A: As follows:

- Pressure.
- Physical character: Colour (clear, purulent, haemorrhagic, straw). If the fluid is kept for 8–12 h, there may be cobweb appearance. Also xanthochromia may be seen.
- Biochemistry: Protein, sugar, chloride.
- Cytology: Cell count, differential count.
- Microbiology: Gram stain, culture and sensitivity, acid fast bacilli (AFB).
- Serology: Viral serology, Venereal Disease Research Laboratory (VDRL), Cryptococcus, etc.
- Polymerase chain reaction (PCR) done in herpes simplex virus, *Mycobacterium tuberculosis*, etc.
- Oligoclonal band on protein electrophoresis.

Q: What are the **characteristics of normal CSF**?
A: As follows:

- Amount: 100–150 ml.
- Pressure: 50–150 mm H_2O on lying, 150–250 mm H_2O on sitting.
- Colour: Clear.
- Protein: 20–40 mg/dL.
- Glucose: 50–80 mg/dL (2/3rd of blood glucose level).
- Chloride: 720–750 mg/dL.
- Cytology: 0–5 cell/cmm (all are lymphocytes).

Q: What are the causes of **raised intracranial pressure**?
A: As follows:

- Meningitis.
- Encephalitis.
- Intracranial space-occupying lesion.
- Benign intracranial hypertension.
- Intracranial haemorrhage.
- Intracranial sinus thrombosis.
- Hydrocephalus.
- Hypertensive encephalopathy.

Q: What are the causes of **decreased intracranial pressure**?
A: As follows:

- Dehydration.
- Spinal block.

Q: What are the **different colours** of CSF?
A: As follows:

- Clear: Normal, viral encephalitis.
- Haemorrhagic: Due to blood (see below).
- Yellow: Xanthochromia (see below).
- Straw: Tuberculosis (cobweb is formed when kept overnight).
- Turbid or cloudy: Pyogenic meningitis.

Q: What are the causes of **blood-stained CSF**?
A: As follows:

- Trauma.
- Subarachnoid haemorrhage.
- Blood leakage from cerebral tumour
- Coagulation disorder (haemophilia, Christmas disease, excess use of anticoagulants, etc.).

Q: How can you **differentiate** traumatic bleeding from subarachnoid haemorrhage?
A: Usually three samples are taken.

Points	Traumatic bleeding	Subarachnoid bleeding
Colour	Initially red, but becomes faint, red or clear in later samples	All the samples are uniformly red
Clot	Present	Absent
Xanthochromia	Absent	Present when kept for some time

Q: What are the causes of **xanthochromia** (yellow colour)?
A: As follows:

- Old subarachnoid haemorrhage.
- Froin syndrome.
- Deep jaundice.

Q: What are the causes of **increased protein** in CSF?
A: As follows:

- Guillain–Barre syndrome.
- Spinal block.
- Acoustic neuroma.
- Froin syndrome.
- Tubercular meningitis.
- Pyogenic meningitis.
- Neurosyphilis (rarely).
- Carcinomatosis.

N.B. Protein level is very high in the first four.

Q: What are the causes of **raised γ-globulin** in CSF?
A: As follows:

- Multiple sclerosis.
- Neurofibromatosis.
- Connective tissue disorder.

Q: What are the causes of **decreased sugar** in CSF?
A: As follows:

- Tubercular meningitis.
- Pyogenic meningitis.
- Hypoglycaemia.
- Carcinomatous meningitis.

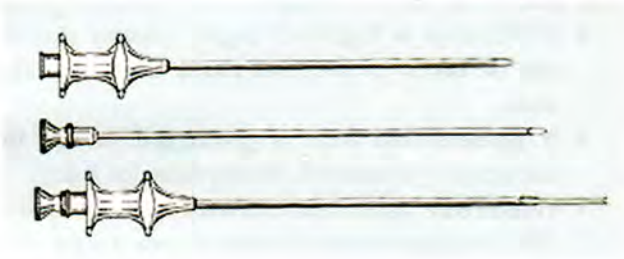
Q: What are the causes of **raised sugar** in CSF?
A: Hyperglycaemia (diabetes mellitus).

Q: What are the causes of **increased lymphocyte** count in CSF?
A: As follows:

- Tubercular meningitis.
- Viral meningitis or encephalitis.
- Neurosyphilis.

Q: What is the cause of **increased neutrophil** count in CSF?
A: Pyogenic meningitis.

Instrument 03: Liver Biopsy Needle



Q: What is this **instrument**?
A: Vim Silverman liver biopsy needle.

Q: What are its **parts**?
A: As follows:

- Cannula.
- Trocar.
- Split needle.

Q: Name different **types of instruments** for liver biopsy.
A: As follows:

- Vim Silverman needle (commonly used).
- Menghini needle.
- Trucut needle.

Q: What are the **indications** of liver biopsy?
A: As follows:

- Chronic liver disease (CLD) (cirrhosis of liver, chronic hepatitis).
- Space-occupying lesions:
 - Hepatic carcinoma.
 - Secondary deposits in liver.
- Metabolic disorder:
 - Haemochromatosis.
 - Wilson disease.
- Infiltrative disease:
 - Sarcoidosis.
 - Lymphoma.
- Amyloidosis.
- Storage diseases (e.g. glycogen storage disease).
- Unexplained hepatomegaly.

Q: What are the **contraindications** of liver biopsy?
A: As follows:

- Bleeding disorder, e.g. haemophilia, Christmas disease.
- Hydatid cyst.
- Passive venous congestion of liver.
- Extrahepatic cholestasis or biliary obstruction.
- Severe jaundice.
- Hepatic encephalopathy (the patient may develop coma).

Q: What **prerequisites** should be taken before doing liver biopsy?
A: As follows:

- The patient should be cooperative, consent should be taken.
- To be excluded: Biliary obstruction, marked ascites, severe anaemia and high bilirubin.
- Prothrombin time should not be >4 of control.
- Platelet count should not be <1,00,000/cmm.
- Blood grouping and cross matching.

Q: How to be sure that the **needle is in the liver**?
A: After introducing the needle, the patient is asked to take deep breath in and out. The needle will move with respiration.

Q: What are the **causes of failure** of liver biopsy?
A: As follows:

- Faulty technique.
- Severe fibrosis of liver.

Q: How to do the **follow-up** after biopsy?
A: As follows:

- The patient should be in complete bed rest for 24 h.
- Regular monitoring of pulse, BP.
- Blood should be kept ready for transfusion.

Q: What are the **complications**?
A: As follows:

- Bleeding.
- Shock.
- Secondary infection.
- Injury to colon and other viscera.
- Pleurisy.
- Pneumothorax.
- Biliary peritonitis.
- May precipitate hepatic encephalopathy in pre-existing liver disease.
- Intrahepatic arteriovenous (AV) fistula.

Q: What are the **methods** of liver biopsy?
A: As follows:

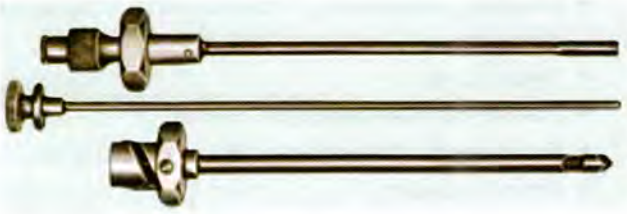
- Percutaneous (better ultrasonography (USG) guided).
- Transjugular.
- Laparoscopic or laparotomy (if done for other reason).

Q: What are the indications of **transjugular liver biopsy**?
A: It is done if there is massive ascites, coagulation abnormality or small, shrunken liver.

N.B. Remember the following:

- If bilirubin is high (>3 mg%), biopsy should not be taken as the liver tissue does not take stain.
- If prothrombin time is prolonged, it can be corrected by vitamin K, 10 mg daily for 3 days.
- Fine-needle aspiration cytology (FNAC) under USG guidance is more preferred now-a-days.

Instrument 04: Pleural Biopsy Needle



Q: What is this **instrument**?
A: Abram pleural biopsy needle.

Q: What are its **parts**?
A: As follows:

- The outer part with a cutting groove into which tissue is taken.
- A solid stylet.
- A cutting trocar.

Q: What is the **procedure**?
A: Pleural biopsy should be taken during aspiration of pleural fluid with this needle. Under local anaesthesia, the needle is introduced after giving a small incision through the skin at the intercostals space. Stylet is removed and pleural fluid is aspirated. Then the cutting trochar is introduced and parietal pleura is cut. The needle is then removed, reopened and the specimen is taken out for histopathology.

Q: What are the **indications**?
A: As follows:

- Malignant pleural effusion.
- Tuberculous pleural effusion.
- Pleural effusion of unknown aetiology.

N.B. In tuberculosis, AFB is positive in pleural fluid in 20% cases and pleural biopsy is positive in 80% cases. In malignancy, pleural biopsy is positive in 40% cases (may be up to 60% cases).

Instrument 05: Aspiration Needle with Rubber Tube



Q: What is this **instrument**?
A: Aspiration needle with rubber tube.

Q: What are its **parts**?
A: Wide-bore needle with rubber tube.

Q: What are the **uses**?
A: Aspiration of pleural fluid, ascitic fluid, pericardial fluid, liver abscess, etc.

N.B. If aspiration needle is not available, aspiration can be done by wide-bore blood-set needle connected to any rubber tube, which is connected with an empty saline bag. Fluid comes out easily by negative suction.

Pleural Fluid Aspiration

Q: What are the **sites** of aspiration of pleural fluid?
A: It is usually done through the 6th intercostal space in the midaxillary line or 8th intercostal space in the posterior scapular line. Clinically, it should be done at the site of maximum dullness.

Q: What are the **indications** of pleural fluid aspiration?
A: As follows:

1. Diagnostic: To diagnose the cause of pleural effusion (tuberculosis, malignancy).
2. Therapeutic:
 - Massive effusion especially with severe respiratory distress or cardiorespiratory embarrassment.
 - Introduction of drugs like talc, kaoline, tetracycline, etc. for chemical pleurodesis (to prevent recurrence of effusion or pneumothorax).
 - Introduction of bleomycin in malignant effusion.

Q: What are the **complications** of pleural fluid aspiration?
A: As follows:

- Iatrogenic pneumothorax (hydropneumothorax).
- Infection may cause empyema.
- Acute pulmonary oedema.
- Injury to neurovascular bundle.
- Vasovagal attack due to fear or severe pain (pleural shock).

Q: How to avoid injury to **neurovascular bundle**?
A: The needle should be inserted near the upper border of the lower rib.

Q: How to avoid **acute pulmonary oedema**?
A: To avoid pulmonary oedema, more than 1 L of fluid should not be removed.

N.B. Remember the following:

- If more than 1–1.5 L of fluid is taken out or fluid is taken out very rapidly, there may be pulmonary oedema. It is due to rapid expansion of the compressed lung that causes leakage of fluid from the pulmonary vessels.
- If the patient complains of cough or respiratory distress or tightness of the chest, aspiration should be stopped.
- After aspiration, a check X-ray should be done to see the amount of fluid or any development of pneumothorax.

Q: What are the causes of **failure** of aspiration of pleural fluid?
A: As follows:

- Faulty technique.
- Encysted effusion (in such case, USG or CT-guided aspiration is more preferable).
- Thick fluid like empyema.

Q: What should be done after taking the **pleural fluid**?
A: As follows:

- Physical character: Colour (clear, straw, haemorrhagic, purulent, chylous).
- Gram staining, cytology (routine) and exfoliative cytology (malignant cell).
- Biochemistry: Protein, sugar [simultaneous blood sugar, protein and lactate dehydrogenase (LDH) may be done].
- Culture and sensitivity (C/S).
- AFB and mycobacterial C/S (in some cases).
- Adenosine deaminase (ADA).
- Other tests according to suspicion of cause (amylase, cholesterol, LDH).

Ascitic Fluid Aspiration

Q: What is the **site** of aspiration of ascitic fluid?
A: At the right iliac fossa, just outside the spinoumbilical line or at the flank.

Q: **How much** fluid can be removed?
A: About 3–5 L of fluid may be drained daily.

Q: What are the **indications** of ascitic fluid aspiration?
A: As follows:

- Diagnostic: To find the cause of ascites like tuberculosis, malignancy, infection, etc.
- Therapeutic: Tense ascites causing cardiorespiratory embarrassment, resistant ascites refractory to medical therapy.

Q: What are the **contraindications** of ascitic fluid aspiration?
A: As follows:

- Bleeding disorder.
- Hepatic encephalopathy.

Q: What are the **complications**?
A: As follows:

- Hypovolaemia leading to shock.
- Infection.
- Injury to viscera.
- Hepatic encephalopathy.

Instrument 06: Intravenous Cannula



Q: What is this **instrument**?
A: Intravenous (IV) cannula.

Q: Mention its **uses**.
A: Intravenous administration of any IV fluid, IV injection, TPN (total parenteral nutrition) and blood products.

Q: What are the **complications**?
A: As follows:

- Thrombophlebitis.
- Sepsis.

Q: What **precautions** should be taken to prevent venous thrombosis and embolism?
A: The cannula should be changed every 3–4 days. If kept for more than 3 days, heparin wash should be given.

Instrument 07: Foley Catheter



Q: What is this **instrument**?
A: Bichannel Foley Catheter.

Q: What are the **uses**?
A: As follows:

- Retention of urine.
- Spastic paraplegia.
- Neurogenic bladder.
- Incontinence of urine.
- Unconscious patient.
- Postoperative patient (major abdominal, pelvic or perineal surgery).
- Urinary bladder irrigation.

Q: What are its **complications**?
A: As follows:

- Trauma.
- Infection.
- Blockage of catheter.
- Stone formation, if kept for a long time.

Instrument 08: Nasogastric Tube (Ryle Tube)



Q: What is this **instrument**?
A: Nasogastric tube.

Q: What are the **uses**?
A: As follows:

1. Therapeutic:
 - Nasogastric feeding.
 - Nasogastric suction (e.g. intestinal obstruction, acute abdomen, acute dilatation of stomach, postoperative).
 - Nasogastric medication in comatose patient.
 - Gastric lavage (noncorrosive poisoning).
2. Diagnostic:
 - Aspiration of gastric juice for gastric juice analysis.
 - Aspiration of gastric fluid for toxicological screening.
 - Fasting gastric lavage for AFB in a child suspected of pulmonary tuberculosis.

Q: How can you test whether the instrument has reached the **correct site** or not?
A: By the following:

- Aspiration of gastric content.
- Listening to the sound with stethoscope over the epigastrium made by injecting 20–30 ml of air through the tube.
- Emersion of the tube in water and looking for any bubble (which appears if the tube is in the airway).
- Also, if the tube enters the airway, the patient will cough violently.

Q: Why there is a **metallic bead** at the tip?
A: It helps in smooth passage of the tube by gravitational force. It also helps to localize the position of the tube in the stomach by X-ray.

Q: What are the **contraindications** of insertion of nasogastric tube?
A: As follows:

- Tracheoesophageal fistula.
- Oesophageal atresia.

Q: If nasogastric tube **cannot be inserted**, what else should be done?
A: Gastrostomy tube should be inserted.

Q: What are the **complications** of nasogastric tube insertion?
A: As follows:

- Cough.
- Aspiration pneumonia.
- Haemorrhage.
- Injury.

Instrument 09: Air Way Tube



Q: What is this **instrument**?
A: Airway tube (oropharyngeal tube).

Q: What is its **use**?
A: As follows:

- To maintain a clear airway.
- To prevent tongue fall back in unconscious patients.
- To prevent tongue bite in epileptic or unconscious patient.

Q: What are its **complications**?
A: Injury to lip, gum, tongue, palate, pharynx, etc.

Instrument 10: ESR Tube



Q: What is this **instrument**?
A: Westergren erythrocyte sedimentation rate (ESR) tube with ESR stand.

Q: What are the **markings** in this tube?
A: It is graduated from 0 to 200 mm.

Q: What are the **methods** of measuring ESR?
A: As follows:

- Westergren method.
- Wintrobe method.

Q: What is the **normal value** of ESR?
A: 0–8 mm in 1st hour in male and 0–12 mm in 1st hour in female.

Q: What are the causes of **raised ESR**?
A: As follows:

- Physiological: Pregnancy.
- Tuberculosis.
- Multiple myeloma.
- Aplastic anaemia.
- Connective tissue disorder:
 - Systemic lupus erythematosus (SLE).
 - Acute rheumatic fever.
 - Rheumatoid arthritis.
 - Polymyalgia rheumatica.
- Giant cell arteritis.

Q: What are the causes of **very-high** (>100) ESR?
A: As follows:

- Multiple myeloma.
- Giant cell arteritis.
- Polymyalgia rheumatica.
- SLE.
- Acute rheumatic fever.

Q: What are the causes of **decreased ESR**?
A: As follows:

- Polycythaemia due to any cause.
- Afibrinogenaemia.

Q: What is the **significance** of ESR?
A: As follows:

- ESR has no specific diagnostic significance. However, it can support a diagnosis.
- It may indicate response to therapy and prognosis.

Instrument 11: Metered-Dose Inhaler



Q: What is this **instrument**?
A: Metered-dose inhaler.

Q: What are its **parts**?
A: As follows:

- Canister.
- Actuator.
- Nozzle.

Q: Name two important **conditions** where this device is used.
A: As follows:

- Bronchial asthma.
- Chronic obstructive pulmonary disease (COPD).

Q: Name some important **drugs** delivered through this device.

A: As follows:

- Salbutamol.
- Steroid.
- Ipratropium bromide.

Q: Name one **complication** of the use of a steroid inhaler.

A: Oral candidiasis (also husky voice).

Q: How would you **prevent** it?

A: I will advise the patient to wash oral cavity after using inhaler containing steroid preparation.

Instrument 12: Accuhaler



Q: What is this **instrument**?

A: Accuhaler.

Q: Name two **conditions** where this device is used.

A: As follows:

- Bronchial asthma.
- COPD.

Q: Name some important **drugs** delivered through this device.

A: As follows:

- Salmeterol.
- Fluticasone.
- Salmeterol plus fluticasone.

Q: What are its **advantages** over metered-dose inhalers?

A: As follows:

- This device is easier to use than conventional metered-dose inhalers, which require careful coordination.
- A numerical dose counter helps monitor the asthma therapy.
- More environment friendly.

Q: What are the **disadvantages**?

A: It may be difficult to use for young children or adults who are short of breath.

Instrument 13: Evohaler



Q: What is this **instrument**?

A: Evohaler.

Q: Name two **conditions** where this device is used.

A: As follows:

- Bronchial asthma.
- COPD.

Q: Name some important **drugs** delivered through this device.

A: As follows:

- Beta agonist like salmeterol, salbutamol.
- Steroid like fluticasone.
- Combination.

Q: What are its **advantages** over conventional metered-dose inhalers?

A: Evohaler uses HFA 134a as a propellant instead of chlorofluorocarbon (CFC). So this is more environment friendly.

Instrument 14: Peak Flow Meter



Q: What is this **instrument**?
A: Peak flow meter.

Q: What are its **uses**?
A: It is used to monitor the progress of the disease and its treatment in:

- Bronchial asthma.
- COPD.

N.B. Regular measurement of peak expiratory flow rate (PEFR) on waking from sleep, in afternoon and before going to bed demonstrates the wide diurnal variation of airflow limitation in bronchial asthma.

Instrument 15: AMBU Bag



Q: What is this **instrument**?
A: AMBU bag with face mask.

Q: Name its **parts**.
A: As follows:

1. Inlet:
 - Air inlet.
 - Oxygen inlet.
2. Bag proper/rubber bag.
3. Safety valve/one-way valve.
4. Outlet.

Q: Name some **indications** for its use.
A: As follows:

- Cardiopulmonary resuscitation.
- Any respiratory distress.
- Temporarily it can be used before intubation.

Instrument 16: Tongue Depressor



Q: What is this **instrument**?
A: Metallic tongue depressor.

Q: What are the **types**?
A: Metallic, plastic and wooden.

Q: What are the **parts**?
A: As follows:

- Depressor part (broad part, used to depress anterior 2/3rd of the tongue).
- Holding part.

Q: What are the **uses**?
A: As follows:

- Diagnostic:
 - To examine the oral cavity: Oral ulcer, cleft palate, Koplik spot, etc.
 - To examine the throat: Tonsillitis, pharyngitis, diphtheria, etc.
 - To collect throat swab.
- Therapeutic: Removal of foreign body from posterior part of the tongue and throat.

Q: What are the causes of **white patch** in throat?
A: As follows:

- Acute follicular tonsillitis.
- Diphtheria.
- Oral candidiasis.
- Vincent angina.
- Agranulocytosis.
- Infectious mononucleosis.

Oral Rehydration Salt



Q: What is it?
A: This is oral rehydration salt (ORS).

Q: What is its **composition**?
A: As follows:

Content	Amount
Sodium chloride	3.5 g/L
Potassium chloride	1.5 g/L
Trisodium citrate	2.9 g/L
Glucose	20 g/L

Water to be added: 1 L

Q: What are its **indications**?
A: As follows:

- Acute watery diarrhoea.
- Correction of dehydration.

Q: How long can it be **preserved**?
A: It can be preserved for up to 12 h. It should be discarded after this time.

Q: What is the function of **glucose**?
A: It helps in absorption of sodium chloride.

Q: What are the composition of **rice ORS**?
A: As follows:

- Sodium chloride: 3.5 g.
- Potassium chloride: 1.5 g.
- Sodium bicarbonate: 2.5 g.
- Rice powder: 50 g.
- Water to be added: 1100 ml.

Now, this is not the end. It is not even the beginning of the end. But it is perhaps, the end of the beginning.

– Winston Churchill

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